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Mindfulness-Based Stretching and Deep Breathing Exercises Normalize Serum Cortisol Levels and Reverse Symptoms of PTSD: A Prospective Randomized-Controlled Trial

Sang Hwan Kim

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MINDFULNESS-BASED STRETCHING AND DEEP BREATHING EXERCISES NORMALIZE SERUM CORTISOL LEVELS AND REVERSE SYMPTOMS OF PTSD: A PROSPECTIVE RANDOMIZED-CONTROLLED TRIAL

by

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DISSERTATION

Submitted in Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

Physical Education, Sports, and Exercise Science

The University of New Mexico
Albuquerque, New Mexico

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Acknowledgements

*This dissertation is dedicated to soldiers, war veterans, nurses, care-givers, victims of inevitable life events, survivors, and those who walk the life of extreme stress.*

The journey thus far has not been a lone one. I owe much to my teachers and family, friends and colleagues. The decision I made at my 49th birthday to pursue a doctoral degree in exercise science was a tough one, and then soon I found things got much tougher. Even tougher was when I was accepted to the Clinical and Translational Science research program at the UNM medical school. Throughout, without the support and inspiration from my teachers, the journey could have hardly been enjoyable. I would like to thank Drs. Len Kravitz, Suzanne M. Schneider, and Christine Mermier for keeping me on track in the academic and personal growth paths. Special thanks go to Drs. Gloria Napper-Owen and Todd Seidler for providing me with conceptual role models as a responsible physical educator for health promotion.

While spending much of the final year in the UNM CTSC doing my dissertation research, I learned how to synthesize various types of knowledge, collaborate with other scientists, and translate theories to clinical applications. Then subsequent challenges were how to write for a grant, organize a research team, conduct the research, analyze the results, and publish the findings. I would like to thank Drs. Mark R. Burge (PI for my dissertation research), Clifford Qualls (biostatistician), and Donald Partridge (my mentor in neuroscience), as well as faculty members of the UNM Clinical and Translational Science programs. At CTSC, Michael Briggs, Cindy Wooten, Danielle Trujillo, Bambi Wolf and CTSC staff were a force in nurturing me to succeed in this NIH/CTSC funded clinical trial.
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My deepest thanks go to my parents: my dad was WWII and Korean War veteran who suffered most of his adult life from PTSD and alcoholism. My mom was like a phoenix who rose from the war-torn family and raised five children successfully while care-giving for my dad. Finally, I must thank my wife Cynthia for her unconditional love and support no matter how odd the ideas I bring up, one of which was certainly to be doing PhD work after 50, and to our daughter Jessica for her youthful push for her dad to race to the finish line. I love you!
Mindfulness-based Stretching and Deep Breathing Exercises Normalize Serum Cortisol Levels and Reverse Symptoms of PTSD: A Prospective Randomized-Controlled Trial

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ABSTRACT

Context: Cortisol, the human glucocorticoid, plays a key role in the pathophysiology of posttraumatic stress disorder (PTSD). It is known that individuals with chronic PTSD suffer from low basal cortisol levels. Endogenic normalization of basal cortisol concentration through exercise may have a therapeutic effect on treating PTSD symptoms, yet little is known about the association between exercise-induced endogenic increase of cortisol and PTSD symptom reduction. Objective: To identify whether mindfulness-based stretching and deep breathing exercise (MBX) increases basal cortisol levels, examine if MBX reduces PTSD symptom severity, and evaluate MBX as a complementary intervention for PTSD. Design: Prospective, randomized, controlled.

Setting: University of New Mexico Hospital. Participants: 29 nurses with PTSD symptoms, ages 45-53, with 28 female. Intervention: 8-week bi-weekly 60-minute MBX
sessions. **Main Outcome Measures:** Serum cortisol and PTSD Checklist-Civilian version (PCL-C) at weeks 0, 4, 8, 12, and 16. **Results:** Twenty-eight participants completed the study procedures. In EX group, serum cortisol levels increased significantly from 9.6±4.1 μg/dl at baseline to 14.6±5.7 μg/dl at week 8 \( (p=0.0039) \); PTSD symptom severity decreased significantly from PCL-C scores of 43.1±11.2 at baseline to 24±3.3 at week 8 \( (p=0.0002) \); and the effects were maintained at follow-up at week 16 with cortisol concentration of 14.0±3.9 μg/dl \( (p=0.5706) \) and PCL-C scores of 25.0±5.1 \( (p=0.8013) \). **Conclusions:** The results indicate a strong relationship between changes in cortisol levels and changes in PTSD symptom severity. This study provides preliminary evidence that programs aimed at reducing symptom severity in individuals with chronic PTSD should consider a mind-body intervention. To our knowledge, this is the first randomized controlled trial to assess the therapeutic benefits of MBX in individuals with PTSD symptoms using both biomarkers and PCL-C scores measuring the long-term effects of cortisol changes.
# TABLE OF CONTENTS

Acknowledgement .................................................................................. iv

Abstract ................................................................................................. vi

Table of Contents .................................................................................... ix

CHAPTER I: INTRODUCTION ................................................................. 1

  Background .......................................................................................... 1

  Statement of the Problem ................................................................. 2

  Purpose of the Study .......................................................................... 3

  Need for the Study ............................................................................ 4

  Hypotheses .......................................................................................... 5

  Assumptions ....................................................................................... 6

  Limitations .......................................................................................... 6

  Significance of the study .................................................................. 6

  Definitions of Terms ......................................................................... 8

  List of Abbreviations .......................................................................... 11

  References .......................................................................................... 12

CHAPTER II: REVIEW OF THE LITERATURE ...................................... 17

  Abstract ............................................................................................. 20

  Introduction ......................................................................................... 21

  Materials and Methods ..................................................................... 21

    Study Inclusion Criteria ................................................................... 22

    Search Strategy ................................................................................ 22

    Inclusion Criteria ............................................................................ 22
Methodological Quality Grade ..................................................22
Results .........................................................................................23
Studies on PTSD Symptom Severity .........................................24
Studies on Vagal Activity ..........................................................27
Discussion ....................................................................................28
Lasting Effects of Short-term Mind-body Practices ..................28
Time, Age, and Gender Factors for PTSD Treatment ...............29
Parasympathetic Regulation .....................................................30
Clinical Implications of Mind-body Interventions ....................30
Limitations ..................................................................................31
Conclusions ................................................................................32
Tables ..........................................................................................33
Figures .........................................................................................36
References ....................................................................................40
CHAPTER III: RESEARCH MANUSCRIPTS .................................43
Abstract .....................................................................................44
Introduction ..................................................................................46
Materials and Methods ...............................................................52
Human Subjects and Study Protocols .......................................52
Mind-body Intervention .............................................................53
Study Design and Randomization .............................................53
Cortisol, ACTH and DHEAS .......................................................54
PCL-C Scores ...............................................................................54
Appendix D: Medical History Questionnaire ........................................ 96
Appendix E: PAR-Q & YOU ................................................................. 98
Appendix F: PCL-C Form ................................................................. 99
Appendix G: AUDIT ........................................................................ 100
Appendix H: DUDIT ....................................................................... 101
Appendix I: Referral Form ............................................................... 103
Appendix J: Emergency Risk Evaluation Protocol ............................. 104
Appendix K: Study Flyer ................................................................. 106
Appendix L: Home Exercise Log ....................................................... 107
Appendix M: Exercise Protocol ......................................................... 108
CHAPTER I: INTRODUCTION

Background

Posttraumatic Stress Disorder (PTSD) is a chronic anxiety disorder (National Center for PTSD 2011) that can occur in individuals who have been exposed to or have witnessed a traumatic experience of an extreme nature (APA 2000). PTSD is characterized by re-experiencing, hyperarousal, and avoidance, with persistent symptoms of increased arousal in the autonomic nervous system (APA 2000) and somatic disturbance (Rothschild 2000). In any given year, 7.7 million Americans over the age of 18 are diagnosed with PTSD (National Institute of Mental Health 2011), a debilitating disorder that is often comorbid with other diseases (Libby 2012). Individuals with PTSD often suffer substantial social and interpersonal problems which may significantly impair many aspects of daily living (Mendlowicz and Stein 2000). Often PTSD patients experience helplessness and a lost sense of self-control in their lives. Difficulties in cognitive, emotional, and physiological processing during trauma have been identified as one important predictor of the development of PTSD (Ozer, Best et al. 2003; Grodin, Piwowarczyk et al. 2008). There is also increasing evidence that chronic PTSD sufferers experience specific, unique neurobiological dysfunctions as a result of the uncontrollable stress associated with the elevated levels of fear and anxiety (Southwick, Krystal et al. 1995) leading to abnormal function in the hypothalamic-pituitary-adrenal (HPA) axis and the Sympathetic-adrenal-medullary (SAM) axis (Boscarino 2004).

In a normal stress response, the SAM pathway stimulates epinephrine (EPI) and norepinephrine (NE) in the adrenal medulla evoking the “fight-or-flight” response, and the HPA pathway triggers the release of cortisol from the adrenal cortex, together
functioning to maintain homeostasis in the human body (Heim and Nemeroff 2009). Repeated stresses, however, evoke dissociation between HPA and SAM responses (de Quervain 2006) and disrupt homeostasis. This dysfunction is manifested in abnormal levels of catecholamines (Yehuda, Southwick et al. 1992) and cortisol (Mason, Giller et al. 1986) in PTSD patients. Recent studies have posited that individuals with PTSD have high catecholamine levels and low plasma and urinary cortisol levels (Yehuda 2003); that low cortisol levels are correlated with PTSD symptom severity (Baker, West et al. 1999); and that cortisol levels may change in relation with symptom modification (Yehuda, Bierer et al. 2009).

Substantial evidence has shown that mind-body practices have a positive impact on stress reduction, quality of life, and improvement of health outcomes among individuals with PTSD. (Barnes 2008; National Institute of Mental Health 2011) In 2010, 39% of individuals with PTSD reported using complementary and alternative medicine interventions, including mind-body exercises that incorporate various types of stretching movements and postures with deep breathing (e.g., yoga, taichi, qigong, and meditation) (Libby 2012).

Statement of the Problem

Current treatments for PTSD focus on reducing symptoms, improving functional capacity and enhancing quality of life through the use of medication, and/or psychotherapy. Other treatment options include Eye Movement Desensitization and Reprocessing (EMDR), Cognitive Behavioral Therapy (CBT), Prolonged Exposure Therapy, Cognitive Processing Therapy, and Stress Inoculation Training. While
psychotherapeutic and pharmacological interventions have some proven efficacy in the management of PTSD symptoms (Grodin, Piwowarczyk et al. 2008; Lawrence, De Silva et al. 2010), residual symptoms remain problematic. Current research has succeeded in identifying treatments that lead to symptom reduction and also in quantifying the neurobiological markers associated with PTSD symptom severity. For example, lasting neurobiological changes in combat veterans with PTSD correlate with the manifestation of specific symptoms including: increased 24-hour urinary norepinephrine positively correlated with intrusive traumatic memories (Southwick, Bremner et al. 1999); and low 24-hour urinary cortisol levels correlated with a failure of normal memory consolidation (Yehuda 2002c). Despite the advances made in the areas of pharmacology, psychotherapy, and biology as they relate to PTSD, we still lack a complete understanding of the anomalies of the autonomic nervous system in PTSD.

Recent studies have shown that low- to moderate-intensity mindfulness-based exercise, such as tai chi or yoga, has positive effects on PTSD symptoms (Telles, Naveen et al. 2007) including significant reductions in reported sleep disturbances, flashbacks and anger outbursts (Brown and Gerbard 2005; Telles, Naveen et al. 2007; Grodin, Piwowarczyk et al. 2008). In healthy individuals, exercise induces a transient increase in cortisol (Brandenberger and Follenius 1975). However, the mechanisms of exercise-induced neurophysiologic changes in PTSD patients are not yet clearly understood. Furthermore, it is not yet clear if there is a link between exercise-induced PTSD symptom reduction and a change in cortisol levels.

**Purpose of the Study**
The primary purpose of this study is to evaluate the relationship between exercise-induced changes in plasma cortisol levels and changes in PTSD symptoms as they occur during an 8-week program of mindfulness-based stretching and breathing exercises compared to a wait-list control group.

Need for the Study

In any given year, 7.7 million Americans over the age of 18 are diagnosed with posttraumatic stress disorder (PTSD) (National Institute of Mental Health 2011). In a recent study of over 100,000 Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) veterans seen at VA health care facilities between September 30, 2001 and December 31, 2005, 25% received mental health diagnoses (Seal, Bertenthal et al. 2007). PTSD represented 52% of these mental health diagnoses, making it the most commonly diagnosed mental health issue among returning veterans (Seal, Bertenthal et al. 2007). As greater numbers of combat veterans return home, PTSD has been an increasingly urgent mental health issue as well as a source of social stress within military communities and civilian communities with large active and retired military populations.

Furthermore, in a recent study, intensive care unit (ICU) nurses were also found to be at high risk for developing PTSD as a result of repetitive exposure to extreme stressors including high patient mortality and morbidity, daily exposure to traumatic events, and the inability to adjust to extreme environments, with 24% of participating nurses testing positive for PTSD symptoms (Mealer, Shelton et al. 2007). In the workplace, persistent PTSD symptoms lead to reduced job satisfaction and productivity, aversion to work (Gates and Gillespie 2008), and increased absenteeism (Laposa and
Alden 2003) and burnout (Acker 1993). The adverse health consequences of unmanaged PTSD in nurses include headaches, gastrointestinal troubles, insomnia, eating disorders, smoking, addiction, and anger displaced onto coworkers and patients (Gates and Gillespie 2008). Considering the 17% vacancy rate for critical care nurses and a predicted 114,000 vacant critical care nursing positions in the United States by 2015, PTSD may be a significant contributor to the increasing shortage of nurses and an exodus of the ICU nurses (Mealer, Shelton et al. 2007).

Additionally, chronic activation of stress responses has negative effects on stress-associated immune dysregulation (Padgett and Glaser 2003) which, if left untreated, may lead to a high rate of comorbidities of diseases (Boscarino 2004) such as digestive and musculoskeletal disease, metabolic syndrome, cardiopulmonary diseases and depression. Clearly, low cortisol level is related to increased morbidity during illness (Zaloga and Marik 2001) and PTSD is one such case.

Hypotheses

1. Nurses who are positively screened for PTSD and participate in an 8-week program of mindfulness-based stretching and breathing exercises would have greater changes in cortisol levels compared to the wait-list control group.

2. Nurses who are positively screened for PTSD and participate in an 8-week program of mindfulness-based stretching and breathing exercises would have greater changes in PTSD symptom severity compared to the wait-list control group.
3. There would be a positive association between exercise-induced reduction in PTSD symptom severity and changes in cortisol levels as a result of participating in an 8-week program of mindfulness-based stretching and breathing exercises.

Assumptions

1. The nurse PTSD patients in this sample are representative of nurse PTSD patients throughout the United States.
2. Medical History Questionnaire, PAR-Q, and PCL-C were truthfully reported.
3. All instruments and cortisol analyses used in this study have high validity and reliability.
4. The participants followed instructions regarding exercise, diet, and medications prior to assessment.

Limitations

This study may be subject to the following limitations:

1. Testing effects: Because the PCL-C instrument will be repeatedly used at 5 time points, we expect practice, familiarity or other forms of reactivity that could be taken for treatment effects causing threat to internal validity. The PCL-C, however, has high internal validity.
2. Generalizability: Since the participants are recruited from the UNM nurses only, the results may not be applicable to the entire PTSD population in the United States.

Significance of the study
We currently lack a clear understanding of the effects of PTSD on the physiological and neurobiological dysregulation of the autonomic nervous system. Studies evaluating the effect of yoga, taichi, and qigong exercises have demonstrated PTSD symptom reduction, including significant reductions in reported sleep disturbances, flashbacks and anger outbursts (Brown and Gerbard 2005; Telles, Naveen et al. 2007; Grodin, Piwowarczyk et al. 2008). In healthy individuals, exercise induces a transient increase in cortisol (Brandenberger and Follenius 1975). It is not yet clear if there is a link between exercise-induced PTSD symptom reduction and a change in cortisol level. The contribution of the proposed research will be a better understanding of the relationship between symptom reduction and changes in cortisol level as a result of an exercise intervention. This contribution is significant because it will advance our knowledge about the physiological regulation anomalies of the autonomic nervous system associated with PTSD and will increase our understanding of how exercise improves PTSD symptomology. For example, it is currently unclear whether low cortisol level is a risk factor for PTSD or is low as a result of traumatic events. Making a connection between changes in cortisol levels and PTSD symptoms that result from an exercise intervention will advance our understanding of these complex dichotomies. It is also expected that establishing this link will increase the recognition of exercise as an adjunct PTSD treatment strategy, and improve patient motivation to try exercise as an adjunct to other PTSD treatments. In addition, the research will be of significance because exercise has the potential to positively address common comorbidities of PTSD such as depression, cardiopulmonary diseases, and metabolic syndrome. As a complementary therapy, exercise may improve current evidence-based psychotherapies and contribute to
more effective treatment of PTSD and greater improvement in quality of life at minimal additional expense. This comparative study can elucidate the added value of an exercise intervention by directly comparing changes in cortisol and symptom severity between the treatment-as-usual group and the treatment-as-usual plus exercise group.

Definitions of Terms

The terms used in the study are defined as follows:

**Adrenal medullae:** Located at the center of the adrenal gland surrounded by the adrenal cortex, consisting of cells that secrete epinephrine and norepinephrine. On the average, approximately 80% of the secretion is epinephrine and 20% is norepinephrine (Guyton 1991).

**Anxiety disorder:** Any of a group of mental conditions that include panic disorder with or without agoraphobia, agoraphobia without panic disorder, simple (specific) phobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, acute stress disorder, generalized anxiety disorder, anxiety caused by a general medical condition, and substance-induced anxiety disorder (Venes 2009).

**Autonomic nervous system:** Part of the peripheral nervous system that controls visceral functions affecting heart rate, digestion, respiration rate, salivation, perspiration, diameter of the pupils, urination, and sexual arousal. It is divided into the parasympathetic nervous system and sympathetic nervous system.

**Catecholamines:** Hormones released by the adrenal glands in response to stress, including epinephrine, norepinephrine and dopamine.
**Cognitive Behavioral Therapy (CBT):** A form of psychotherapy that aims to solve problems concerning dysfunctional emotions, behaviors and cognitions through a goal-oriented, systematic procedure in the present. CBT is reported to be somewhat superior to antidepressants in the treatment of adult depression, and is equally effective as behavior therapy in the treatment of adult depression and obsessive-compulsive disorder (Butler, Chapman et al. 2006).

**Cortisol:** A glucocortical hormone of the adrenal cortex, usually referred to pharmaceutically as hydrocortisone, and closely related to cortisone in its physiological effects (Venes 2009). Cortisol is released in response to stress increasing blood sugar via gluconeogenesis, suppressing the immune system, and metabolized in the liver with a half-life of 60-90 minutes in the circulation.

**DSM-IV:** Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, a manual published by the American Psychiatric Association (APA) that includes all currently recognized mental health disorders.

**Eye Movement Desensitization and Reprocessing (EMDR):** A controversial method of psychotherapy used for treating posttraumatic stress syndrome and anxiety disorders, using a very short-term therapy for treating trauma victims that utilizes rhythmical stimulation such as eye movements or hand taps (Shapiro 1998).

**Epinephrine (EPI):** A hormone, secreted by the adrenal glands during the fight-or-flight response of the sympathetic nervous system, increases heart rate, constricts blood vessels, and dilates air passages.

**Hypothalamic-pituitary-adrenal (HPA) axis:** A complex set of neuroendocrine feedback systems among the hypothalamus, the pituitary gland, and the adrenal glands,
regulating reactions to stress and many bodily processes such as digestion, the immune system, mood and emotions, and energy balance. HPA activity is shaped by a person's response to the situation: a blunted hormonal response to stress may predispose a person to develop PTSD (e.g., cortisol increases with subjective distress but is lower in persons with PTSD) (Miller, Chen et al. 2007).

**Norepinephrine (NE):** A stress hormone and a neurotransmitter released from the sympathetic neurons increasing the rate of cardiac contractions and blood flow to the muscles, triggering the release of glucose from energy stores (Guyton 1991), and affecting parts of the brain, such as the amygdala, where attention and responses are controlled (Tanaka, Yoshida et al. 2000).

**PAR-Q:** The Physical Activity Readiness Questionnaire, a self-screening tool used prior to starting an exercise program to determine the safety or possible risk of exercising for an individual based upon their answers to specific health-related questions.

**PCL-C:** Posttraumatic Stress Disorder Checklist - Civilian version, a 17-item self-report measure of the 17 DSM-IV symptoms of PTSD used for screening individuals for PTSD, diagnosing PTSD, and monitoring symptom change during and after treatment.

**Posttraumatic Stress Disorder (PTSD):** A chronic anxiety disorder that can occur in individuals who have been exposed to or have witnessed a traumatic experience of an extreme nature (APA 2000). PTSD is characterized by re-experiencing, hyperarousal, and avoidance, with persistent symptoms of increased arousal in the autonomic nervous system (APA 2000) and somatic disturbance (Rothschild 2000).

**Qigong:** A mind–body exercise originating from traditional Chinese medicine combining meditation, controlled breathing and gentle, physical movements designed to direct
mental attention to specific areas of the body (Posadzki, Parekh et al. 2010) aiming to improve health by reducing stress, anxiety, and depression as well as to improve physical activity and balance (Stenlund, Ahlgren et al. 2009).

**Sympathetic-adrenal-medullary (SAM) axis:** The SAM pathway, often equated with the sympathetic nervous system (SNS) and under the control of the central nervous system (CNS), elicits the desired fight or flight mode by sending a signal to the adrenal medulla via the spinal cord, triggering the secretion of epinephrine and norepinephrine and preparing the nervous system to respond to a threat (Cannon 1914).

**List of Abbreviations**

CBT = Cognitive Behavioral Therapy
EMDR = Eye Movement Desensitization and Reprocessing
EPI = Epinephrine
HPA axis = Hypothalamic-pituitary-adrenal axis
ICU = Intensive care unit
NE = Norepinephrine
OEF = Operation Enduring Freedom
OEI = Operation Iraqi Freedom
PAR-Q = Physical Activity Readiness Questionnaire
PCL-C = Posttraumatic Stress Disorder Check List - Civilian version
PTSD = Posttraumatic Stress Disorder
SAM axis = Sympathetic-adrenal-medullary axis
VA = Veterans Affairs
References


APA (2000). Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR.


CHAPTER II: LITERATURE REVIEW

This chapter presents a review manuscript that was submitted to and accepted by the Journal of Investigative Medicine under the condition of appropriate revision. The references cited in this review are provided at the end of the manuscript. A review of literature is also included in this chapter.
Literature Review: Mind-body Practices for Posttraumatic Stress Disorder

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Key Words: mindfulness, exercise, breathing, yoga, taichi, posttraumatic stress disorder

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A Review: Mind-body Practices for Posttraumatic Stress Disorder

ABSTRACT

Background: Mind-body practices are increasingly used to provide stress reduction for posttraumatic stress disorder (PTSD). Methods: This is a literature review using PubMed, PsycINFO, and PILOTS to identify the exercise components of mind-body practices such as yoga, taichi, qigong, mindfulness-based stress reduction, meditation, and deep breathing as interventions for PTSD. Results: The literature search identified 92 articles. We reviewed only original, full text articles that met the inclusion criteria. Most of the studies have small sample size, but findings from the 12 publications reviewed here suggest that mind-body practices are associated with positive impacts on PTSD symptoms. Mind-body exercise incorporates numerous therapeutic effects on stress responses, including dramatic reductions in anxiety, depression, and anger, and increases in pain-tolerance, self-esteem, energy levels, ability to relax, and ability to cope with stressful situations. In general, mind-body exercise was found to be a viable intervention to improve the constellation of PTSD symptoms such as intrusive memories, avoidance, and increased emotional arousal. Conclusions: Mind-body exercise is increasingly employed in the treatment of PTSD and is associated with positive impacts on stress-induced illnesses such as depression and PTSD. Knowledge about the diverse modalities of mind-body practices may provide clinicians and patients with the opportunity to explore an individualized and effective treatment plan enhanced by mind-body practice as part of ongoing self-care.
Introduction

Posttraumatic stress disorder (PTSD) is an anxiety disorder that results from exposure to a traumatic event. (APA, 1987) In any given year, 7.7 million Americans over the age of 18 are diagnosed with PTSD, (National Institute of Mental Health, 2011) a debilitating disorder that is often comorbid with other diseases. (Libby, 2012) Individuals with PTSD suffer substantial social and interpersonal problems, as well as impaired quality of life stemming from the long-term presence of the intrusive, avoidant and hyperaroused symptoms that characterize the disease. Although pharmacological and cognitive therapy interventions have some proven efficacy in the treatment of PTSD, (Grodin, Piwowarczyk, Fulker, Bazazi, & Saper, 2008) residual symptoms remain problematic.

Substantial evidence has shown that mind-body practices have a positive impact on quality of life, stress reduction, and improvement of health outcomes among individuals with PTSD. (Barnes, 2008; National Institute of Mental Health, 2011) In 2010, 39 percent of individuals with PTSD reported using complementary and alternative medicine (CAM) interventions, including mind-body practices that incorporate various types of stretching movements and postures with deep breathing (e.g., yoga, taichi, qigong, and meditation). (Libby, 2012) However, the neural and biological mechanisms that underlie a mind-body approach to managing PTSD symptoms are not well delineated. The purpose of this article is to review the evidence that supports the effectiveness of mindfulness-based strategies.

Materials and Methods
Study Inclusion Criteria

We searched for peer-reviewed original journal articles in English on the effects of a mindfulness-based approach to treat PTSD. We included demographics, PTSD symptoms (i.e., intrusive thought, flashback, avoidance, numbness, hyperarousal), and heart rate variability (HRV) as variables.

Search Strategy

Our literature searches of PubMed/MEDLINE, EBSCO/PsycINFO, and the Published International Literature on Traumatic Stress (PILOTS) database took place on March 5th, 2012. We used combinations of the search terms “mindfulness” or “mind-body”, and “exercise” or “yoga” or “taichi” or “qigong” or “meditation” and “posttraumatic stress disorder” or “PTSD”.

Inclusion Criteria

We initially screened abstracts published in English that included human participants with PTSD. Those abstracts included randomized control trials, comparative studies, and observational studies that evaluated the efficacy of mind-body interventions on PTSD symptom changes. For articles that passed the initial screening, we retrieved the full articles to assess eligibility.

Methodological Quality Grade

For critical appraisal of the literature reviewed for the study, we used a methodological quality assessment of ten questions adapted from Young and Solomon
To assign a nominal quality grade for the selected studies, we used a three category grading system of A, B, and C which we adapted from the Evidence-based Practice Centers (EPCs) of the Agency for Healthcare Research and Quality (AHRQ). Category A articles have valid outcomes, the least bias, adequate methods to assess the intervention, clear inclusion and exclusion criteria, and clear descriptions of the study population, setting, interventions and comparison groups. Category B articles have some bias but not a sufficient amount to invalidate the outcomes, as well as some of the deficiencies in the criteria for category A and/or missing data. Category C articles have significant biases that may invalidate the outcomes, serious errors in study design and analysis, and/or a large amount of missing data.

Results

We screened 92 English language abstracts and selected for review a total of 12 articles that met the inclusion criteria (Figure 1). Four randomized controlled trials (RCT), 7 non-randomized studies (NRS), and 1 observational noncontrolled study (OBS) with a total of 824 participants were selected for review (Table 2). Seventy-six publications did not meet the inclusion criteria: 27 articles were unrelated to the study subject, 9 were from book chapters, 7 were dissertations, 22 were editorials or reviews, and 12 journals were unavailable. Twenty-six articles overlapped across more than two search engines. Two articles were available only in PubMed. Of the 12 studies reviewed, two examined the effects of yoga; three the effects of meditation, or meditation and relaxation; one the effects of taichi and qigong; two the efficacy of mindfulness-based
stress reduction (MBSR); one the effects of relaxation, or relaxation plus deep breathing, or relaxation plus deep breathing and thermal biofeedback; and three studies examined the effects of mind-body skills (a combination of various mindfulness-based approaches). Ten studies reported significant positive effects of mind-body practices on reduction of PTSD symptoms via regulation of the sympathetic and/or parasympathetic nervous systems (Table 3). Seven studies did not have a control group. Of the 12 reviewed articles, 4 received an A quality score, 5 received a B score, and 3 received a C score (Table 2). Studies that received a C score had a significant amount of missing data.

Studies on PTSD Symptom Severity

Although there were several common elements in the reviewed studies, such as mindfulness, exercise, meditation, and deep breathing, the outcome parameter for assessing “changes in PTSD symptom severity” varied. The common measures of symptom severity were performed using self-rated instruments such as the PTSD CheckList (PCL), the Harvard Trauma Questionnaire (HTQ), the UCLA PTSD Index for DSM-IV (UPID), the PTSD Reaction Index (PTSD-RI) and the Child PTSD Symptom Scale (CPSS). Of the 12 reviewed studies (Table 2), two studies showed no statistically significant outcomes, (Telles, Singh, Joshi, & Balkrishna, 2010; Watson, Tuorila, Vickers, Gearhart, & Mendez, 1997) and 10 studies showed a significant decrease of PTSD symptom severity as a result of participation in a mind-body intervention. (Catani et al., 2009; Descilo et al., 2010; J S Gordon, Staples, Blyta, & Bytyqi, 2004; J. S. Gordon, Staples, Blyta, Bytyqi, & Wilson, 2008; Grodin, et al., 2008; Kearney, McDermott, Malte, Martinez, & Simpson, 2012; Kimbrough, Magyari, Langenberg, Chesney, &
Berman, 2010; Rosenthal, Grosswald, Ross, & Rosenthal, 2011; Staples, 2011; Waelde et al., 2008) In the 10 studies that incorporated follow-up testing ranging from 3 months to 15 months following intervention, positive results were maintained.(Catani, et al., 2009; Descilo, et al., 2010; J S Gordon, et al., 2004; J. S. Gordon, et al., 2008; Grodin, et al., 2008; Kearney, et al., 2012; Kimbrough, et al., 2010; Rosenthal, et al., 2011; Staples, 2011; Waelde, et al., 2008) Six studies reported decreases in specific PTSD symptom clusters including hyperarousal, avoidance, and numbing. (Catani, et al., 2009; J. S. Gordon, et al., 2008; Kearney, et al., 2012; Staples, 2011; Waelde, et al., 2008; Watson, et al., 1997)

The four RCTs share common mindfulness-based components of relaxation, meditation, and deep breathing. Watson and colleagues(Watson, et al., 1997) compared relaxation, relaxation plus deep breathing, and relaxation plus deep breathing and thermal biofeedback. The authors reported pre-test PTSD Index scores of 95.4, 95.0; 98.1, and post-test PTSD Index scores of 97.8; 90.5, 89.4 for relaxation, relaxation plus deep breathing, and relaxation plus deep breathing and thermal biofeedback, respectively, but they found no significant difference between groups (Table 3). These results suggest that deep breathing and thermal biofeedback may not have additional therapeutic effects for PTSD. Conversely, Catani and colleagues(Catani, et al., 2009) found that a short-term meditation-relaxation intervention significantly reduced PTSD symptoms. The investigators randomized 31 children into meditation-relaxation (MED-RELAX) or Narrative Exposure Therapy (KIDNET) interventions one month after the Tsunami in the North-Eastern region of Sri Lanka. After 6-sessions conducted over a 2-week period, participation in the MED-RELAX program was associated with a significant reduction in
PTSD symptoms (UPID scores of 36.58 and 12.59, pre- and posttest respectively, Cohen’s d = 1.83) (Table 3). More importantly, these results were as effective as the conventional KIDNET PTSD therapy (UPID scores of 37.94 and 12.41, pre- and posttest respectively, Cohen’s d = 1.76). Furthermore, the 6-month follow-up UPID scores were 9.75 (80% recovery rate) and 12.3 (70% recovery rate) for MED-RELAX and KIDNET respectively, demonstrating the long-term effectiveness of MED-RELAX.

Rosenthal and colleagues (Rosenthal, et al., 2011) also reported that transcendental meditation has a significant positive impact on alleviating PTSD symptoms among veterans returning from Operation Enduring Freedom or Operation Iraqi Freedom with combat-related PTSD (Figure 2A). All subjects (n = 5) showed significant mean reductions in the Clinician Administered PTSD Scale (CAPS) and the PTSD Checklist-Military Version with decreases of 31.4 (p = 0.02) and 24.00 (p < 0.02) points, respectively. Similarly, the RCT conducted in 2008 by Gordon and colleagues (J. S. Gordon, et al., 2008) showed decreases in PTSD symptoms in postwar Kosovar adolescents. The authors randomized 82 high school students into a 12-session mind-body skills program or a wait-list control group. HTQ scores improved significantly (2.5 and 2.0, pre- and posttest, respectively, p < 0.001). These findings were consistent with the results from their previous pilot study in 2004 (Table 2). Furthermore, they reported that all 3 PTSD symptom clusters were significantly reduced after MBSR intervention: re-experiencing (p = 0.001), avoidance and numbing (p < 0.001), and hyperarousal (p = 0.001) (Figure 2B).

Kearney and colleagues reported that 40% of veterans (n = 92) who practiced mindfulness-based stress reduction (MBSR) showed clinically significant reduction in
PTSD symptom severity at two months, the symptom improvement was maintained at the 6-month follow-up (Figure 3A). On the other hand, Staple and colleagues reported that individuals with higher baseline scores of symptom severity showed greater improvement in response to the mind-body skills intervention, but the gains did not entirely persist at follow-up (Figure 3B).

Studies on Vagal Activity

HRV is the cyclic variation in the duration between successive heartbeats. It is used as an index to measure changes in the autonomic nervous system, (Song et al., 2011) and is a reliable marker of vagal (parasympathetic) activity of the heart, as well as stress vulnerability. (Porges, 1995) In general, decreased HRV reflects increased sympathetic regulation and stress,(Dishman et al., 2000) and is associated with increased PTSD symptom severity. (Cohen et al., 1998) One study that examined the relationship between mind-body practice and HRV during the stress response following a natural disaster showed no improvement in Heart Rate Variability among individuals with anxiety. (Telles, et al., 2010) After a month of natural disasters in north India, Telles et al. (2012)(Telles, et al., 2010) assessed 1,089 disaster victims using the Screening Questionnaire for Disaster Mental Health (SQD) to obtain scores for PTSD and depression. Twenty-two participants were randomized into yoga therapy or wait-list control groups. Researchers collected HRV data using frequency domain analysis for very low frequency (VLF) band (0.0-0.04 Hz), low frequency (LF) band (0.5-0.15 Hz), high frequency (HF) band (0.15-0.50 Hz), as well as the LF/HF ratio (Table 3). They also recorded time domain HRV analysis using pNN50, the percentage of successive normal
cardiac interbeat intervals greater than 50 msec. (Telles, et al., 2010) No significant changes were found in the HRV between the groups. Of note, after seven days of yoga training, the yoga group showed a significant decrease in sadness (p < 0.05), and the non-yoga group showed increased anxiety (p < 0.05).

Discussion

This review demonstrates that mind-body practices are currently being used to treat PTSD and that multiple components of such practices may provide therapeutic effects for rapid and sustained relief of PTSD symptoms. (Catani, et al., 2009; Descilo, et al., 2010; J S Gordon, et al., 2004; J. S. Gordon, et al., 2008; Grodin, et al., 2008; Staples, 2011; Telles, et al., 2010; Watson, et al., 1997) Mind-body practices appear to be safe for participants with PTSD, and the observed positive impacts in clinical outcome measures were generally sustained at follow-up. Ten out of twelve studies showed a positive impact of a mind-body approach and demonstrated significant improvements in PTSD symptom severity. The broad range of geographic and demographic elements in the selected studies suggests that mind-body interventions are beneficial across a wide variety of populations.

Lasting Effects of Short-term Mind-body Practices

Considering that early intervention is critical in ameliorating the development of PTSD, (Descilo, et al., 2010) and that PTSD symptoms are strongly correlated with the degrees of distress immediately following the trauma, (Descilo, et al., 2010) short-term mind-body interventions ranging from 2 to 8 weeks may provide a potent
nonpharmacological treatment for individuals with PTSD. Of particular interest is the finding that mediation-relaxation was as effective as Narrative Exposure Therapy for reducing PTSD sympomatology in children.(Catani, et al., 2009) This suggests that in the immediate aftermath of a traumatic event, mind-body exercise may reduce intrusive thoughts of trauma and promote extinction of fear, even in the absence of conventional therapy.(Catani, et al., 2009) Furthermore, despite the short duration of the interventions, the effects of PTSD symptom reduction appear to be long lasting.(Catani, et al., 2009; J. S. Gordon, et al., 2008; Staples, 2011)

Time, Age and Gender Factors for PTSD Treatment

Staples and colleagues(Staples, 2011) demonstrated that following a mind-body intervention, there was a highly significant effect of time, suggesting that early intervention is critical in treating PTSD. They also found that individuals with higher baseline scores showed greater improvements in PTSD, but that higher baseline PTSD symptoms were not correlated with age. Gender had significant effects regarding avoidance symptoms, with male children showing greater improvement in scores from baseline to follow-up than females. Additionally, Waelde and his colleagues(Waelde, et al., 2008) suggested that the total time spent in meditation practice is positively associated with greater improvement in PTSD symptom severity. In summary, it is likely that mind-body interventions for children are highly effective in older children at the early stage of development of PTSD, and that longer practice may have a greater impact in PTSD symptom reduction.
Parasympathetic Regulation

Although PTSD symptom severity is associated with increased heart rate variability, (Cohen, et al., 1998) the one study examining HRV that we reviewed did not find a significant effect of yoga on HRV. In the reviewed study, (Telles, et al., 2010) the absence of change in HRV may be due to the nature of the exercise protocol and the particular breathing techniques applied. Cohen and colleagues (Cohen, et al., 1998) stated that HRV is closely related to the breath rate, (Cohen, et al., 1998) and that fast breathing stimulates the sympathetic nervous system while slow breathing activates vagal activity, leading to reduced psycho-physiologic arousal. The combination of fast and slow breathing used in the study may have failed to influence the HRV, resulting in no significant change, suggesting that slow breathing practice alone may increase parasympathetic function and HRV for individuals with symptomatic PTSD. Further investigation regarding the effect of mind-body exercise and deep breathing may elucidate a relationship between the frequency and depth of breath and vagal activity.

Clinical Implications of Mind-body Interventions

Evidence presented in this review supports mind-body exercise as an efficacious adjunct therapy for the treatment of PTSD. Mind-body practices may contribute to decreasing PTSD symptoms by offering participants opportunities to reduce stress levels, improve mood, reduce the intensity of PTSD arousal symptoms, and observe what they experience from a more relaxed state with less fear and more equanimity in an environment of greater social-support via group-activity. (Staples, 2011) Figure 4 depicts a schematic representation of how patients with PTSD might be apportioned to mind-
body exercises as a component of their therapy, as well as the expected benefits of such an approach.

Individuals with PTSD increasingly use mind-body practices as an alternative or adjunct to conventional care for PTSD. Clinicians should discuss mind-body interventions with their patients and educate them about the benefits of mind-body practice to maximize the diversity of treatment options. (Libby, 2012) Knowledge of modalities of mind-body interventions, and of providers in the community who can direct mind-body intervention, may provide patients with the opportunity to explore individualized self-care therapies. Further studies are warranted to assess the comprehensive effects of the mind-body practices on treating comorbid diseases and improving quality of life.

Limitations

The research methodologies included in this review were heterogeneous, and the quality of the studies varied widely. Due to differences in design, intervention methods, and study duration, as well as the presence or absence of control groups, we were unable to conduct a true meta-analysis. The study by Gordin and colleagues (Grodin, et al., 2008) was the only qualitative research included in this review. Despite the lack of quantitative outcomes, we included the study because of the long study duration (>1 yr) and the significant findings described therein. Most of the studies we reviewed for potential inclusion in the study did not have a control group, and two of the reviewed articles had a large amount of missing data. (Staples, 2011) Attrition was problematic in one study, with 31 percent of the study participants dropping out after baseline data were
collected. (Descilo, et al., 2010) Additionally, the mean ages of study participants ranged from 11.95 to 51 years in the reviewed studies, with predominantly male subjects or a mixture of both genders. Future studies need to include younger or older populations to examine whether the demonstrated efficacy may be generalized, particularly to female subjects.

Conclusions

Future studies need to replicate these findings in other cultural settings with varied populations, preferably with larger samples, an untreated control group, and additional outcome measures such as biomarkers (i.e., cortisol, adrenocorticotropic hormones, epinephrine, and norepinephrine). Elucidation of the relationships between changes in psychological symptoms and changes in the biomarkers will advance our understanding of the nonpharmacologic psycho-biological mechanism(s) of mind-body practices for clinical application. Further research will enable us to validate the role of mind-body practices in preventing and treating PTSD so that these strategies, together with other lifestyle modifications and psychotherapies, become a part of the standard treatment regimen for PTSD in the future.
<table>
<thead>
<tr>
<th>Study</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<th>8</th>
<th>9</th>
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<th>Total score</th>
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<tr>
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<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>y</td>
<td>9</td>
</tr>
<tr>
<td>Descilo et al. 2010</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>y</td>
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<td>9</td>
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<td>Gordon et al. 2004</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>n</td>
<td>9</td>
</tr>
<tr>
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<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>y</td>
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<td>y</td>
<td>n</td>
<td>n</td>
<td>Y</td>
<td>n</td>
<td>6</td>
</tr>
<tr>
<td>Staples et al. 2011</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>n</td>
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<td>Telles et al. 2010</td>
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<td>Y</td>
<td>y</td>
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<td>Watson et al. 1997</td>
<td>y</td>
<td>y</td>
<td>y</td>
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<td>n</td>
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<td>n</td>
<td>Y</td>
<td>n</td>
<td>n</td>
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<td>Waelde et al. 2004</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>Y</td>
<td>n</td>
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<td>Kimbrough et al. 2010</td>
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<td>y</td>
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<td>y</td>
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<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>n</td>
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<td>Rosenthal et al. 2011</td>
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<td>y</td>
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<td>n</td>
<td>Y</td>
<td>n</td>
<td>n</td>
<td>6</td>
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<tr>
<td>Kearney et al. 2012</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>Y</td>
<td>y</td>
<td>10</td>
</tr>
</tbody>
</table>
### TABLE 2. Studies of Mind-body Interventions in Patients with PTSD

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study Site</th>
<th>Mean age (SD)</th>
<th>Gender (%)</th>
<th>Intervention Time Frame</th>
<th>Sample Size</th>
<th>PTSD Outcomes, Magnitude of Symptom Change</th>
<th>Study Quality Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desclo et al.</td>
<td>2010</td>
<td>NRS</td>
<td>Adult 30.8</td>
<td>Female (85)</td>
<td>Yoga breathing</td>
<td>N = 183</td>
<td>60% decrease in PTSD symptom severity at weeks 6, 24</td>
<td>B</td>
</tr>
<tr>
<td>Staples et al.</td>
<td>2011</td>
<td>NRS</td>
<td>Age 8-18</td>
<td>N = 129</td>
<td>Mind-body skills</td>
<td></td>
<td>Significant effect of time for PTSD subscales.</td>
<td>C</td>
</tr>
<tr>
<td>Gaza et al.</td>
<td>2010</td>
<td>RCT</td>
<td>Adult 31.5 (7.5)</td>
<td>Male (100)</td>
<td>Yoga</td>
<td>N = 22</td>
<td>No significant changes in the HRV.</td>
<td>B</td>
</tr>
<tr>
<td>Telles et al.</td>
<td>1997</td>
<td>RCT</td>
<td>Adult 45.6</td>
<td>Male (100)</td>
<td>Relaxation, breathing,</td>
<td>N = 90</td>
<td>Moderate effect of relaxation, but not breathing and/or biofeedback in PTSD treatment.</td>
<td>A</td>
</tr>
<tr>
<td>Catani et al.</td>
<td>2009</td>
<td>RCT</td>
<td>Children 11.95</td>
<td>Male (54.8)</td>
<td>Meditation-relaxation</td>
<td>N = 31</td>
<td>Significant PTSD symptom reduction</td>
<td>B</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>2004</td>
<td>NRS</td>
<td>Adolescents 16-19 (68%)</td>
<td>N = 139</td>
<td>Mind-body skills</td>
<td></td>
<td>Significant PTSD symptom reduction at posttest.</td>
<td>C</td>
</tr>
<tr>
<td>Gordon et al.</td>
<td>2008</td>
<td>RCT</td>
<td>Adolescents 16.3</td>
<td>Female (62)</td>
<td>Mind-body skills</td>
<td>N = 82</td>
<td>Significant decrease in PTSD symptom severity.</td>
<td>A</td>
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<tr>
<td>Kosovo Gorden</td>
<td>2008</td>
<td>OBS</td>
<td>Adult (Foreign patients) &gt;1 year</td>
<td>N = 4</td>
<td>Taichi and Qigong</td>
<td></td>
<td>Decreased re-experiencing, flashbacks, anxiety, and stress</td>
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<tr>
<td>Grodin et al.</td>
<td>2008</td>
<td>Case study</td>
<td>Age = 23, 30, 44, 47</td>
<td>Male (75)</td>
<td>Meditation</td>
<td>N = 20</td>
<td>Increased equanimity</td>
<td>B</td>
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<td>Waelde et al.</td>
<td>2004</td>
<td>NRS</td>
<td>Adult 49 (11)</td>
<td>Female (85)</td>
<td>Relaxation</td>
<td>N = 27</td>
<td>Significant decrease in PTSD symptom severity, stress coping, and frustration tolerance.</td>
<td>B</td>
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<tr>
<td>Kimbrough et al.</td>
<td>2010</td>
<td>NRS</td>
<td>Adult 45 (10.8)</td>
<td>Female (89)</td>
<td>MBRSR</td>
<td>N = 27</td>
<td>PTSD symptom severity improved by 31% after 8-week MBRSR.</td>
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<tr>
<td>Rosenthal et al.</td>
<td>2011</td>
<td>NRS</td>
<td>Adult 41.5 (16.6)</td>
<td>Male (100)</td>
<td>Meditation</td>
<td>N = 5</td>
<td>Significant improvement in PTSD symptom severity.</td>
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<tr>
<td>Kearney et al.</td>
<td>2012</td>
<td>NRS</td>
<td>Adult 51 (10.6)</td>
<td>Male (75)</td>
<td>MBRSR</td>
<td>N = 92</td>
<td>Significant improvement in PTSD symptom severity.</td>
<td>A</td>
</tr>
</tbody>
</table>

Data are shown as mean (SD) for quantitative variables and mean (%) for gender.
Abbreviations: NRS, prospective nonrandomized studies; RCT, Randomized Controlled Trial; CPSS, Child PTSD Symptom Scale; HRV, heart rate variability; pNN50, the percentage of successive normal cardiac interbeat intervals greater than 50 msec; UPID, UCLA PTSD Index for DSM-IV; PTSD-R1, PTSD Reaction Index; HTQ, Harvard Trauma Questionnaire; PCL-S, PTSD Checklist-Specific Version; CAPS, the Clinician Administered PTSD Scale; PCL-M, PTSD Checklist-Military Version.
<table>
<thead>
<tr>
<th>Author</th>
<th>Instrument/Dependent Variable</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>Changes in Mean (%)</th>
<th>P</th>
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<tbody>
<tr>
<td>Desclo et al.</td>
<td>PCL-17/PTSD Symptoms</td>
<td>66.5</td>
<td>23.9</td>
<td>-42.5</td>
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<td>Staples et al.</td>
<td>CPSS total</td>
<td>30.0 (6.8)</td>
<td>13.2 (7.3)</td>
<td>-16.8</td>
<td>0.0001</td>
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<td></td>
<td>CPSS subscales</td>
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<td></td>
<td>Reexperiencing</td>
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<td>3.9 (2.7)</td>
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<td>Avoidance</td>
<td>12.3 (3.0)</td>
<td>5.3 (3.4)</td>
<td>-7.0</td>
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<td></td>
<td>Arousal</td>
<td>9.4 (2.6)</td>
<td>3.9 (2.9)</td>
<td>-5.5</td>
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<tr>
<td>Telles et al.</td>
<td>HRV</td>
<td>56.54</td>
<td>55.76</td>
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<td></td>
<td>Vagal Activity</td>
<td>43.40</td>
<td>44.19</td>
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<tr>
<td></td>
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<td>1.23</td>
<td>1.77</td>
<td>-0.54</td>
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<tr>
<td>Watson et al.</td>
<td>PTSD-I/PTSD Symptom</td>
<td>95.4</td>
<td>95.0</td>
<td>-4.0</td>
<td>&gt;0.05</td>
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<td></td>
<td></td>
<td>81.8</td>
<td>89.4</td>
<td>-8.3</td>
<td></td>
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<tr>
<td>Catani et al.</td>
<td>UPID/PTSD Symptoms</td>
<td>36.58</td>
<td>12.59 (11.06)</td>
<td>-23.99</td>
<td>0.0001</td>
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<td>Gordon et al.</td>
<td>PTSD-R/Psymptoms</td>
<td>8.3</td>
<td>6.1</td>
<td>-2.2</td>
<td>&lt;0.001</td>
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<td></td>
<td>Group II: 10.8</td>
<td>5.8</td>
<td>5.5</td>
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<td>Gordon et al.</td>
<td>HTQ</td>
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<td>Gordon et al.</td>
<td>% of Subjects w/PTSD Reexperiencing</td>
<td>100</td>
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<td>Avoidance/numbing</td>
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<td>Nightmares</td>
<td>Reexperiencing</td>
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<td>Flashbacks</td>
<td>Physical pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased energy</td>
<td>Anxiety and stress</td>
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<td></td>
<td></td>
<td>Helplessness</td>
<td>Increase in:</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Hypervigilance</td>
<td>Equanimity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anxiety</td>
<td>Soothing effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waelde et al.</td>
<td>PCL-S Total</td>
<td>36.60 (9.97)</td>
<td>30.57 (9.75)</td>
<td>-6.03</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>PCL-S subscales</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reexperiencing</td>
<td>8.79 (2.99)</td>
<td>7.33 (2.53)</td>
<td>-1.46</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Avoidance</td>
<td>14.99 (5.59)</td>
<td>13.40 (4.21)</td>
<td>-1.59</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Hyperarousal</td>
<td>12.74 (4.54)</td>
<td>9.80 (3.84)</td>
<td>-2.94</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Kimbrough et al.</td>
<td>PTSD-I/PTSD Symptoms</td>
<td>48.8 (2.7)</td>
<td>32.3 (1.9)</td>
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<td>&lt;0.01</td>
</tr>
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<td>Rosenthal et al.</td>
<td>CAPS/PTSD Symptoms</td>
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<td>39.6</td>
<td>-31.4</td>
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<td>Kearney et al.</td>
<td>PCL-M</td>
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<td>33.8</td>
<td>-24.0</td>
<td>&lt;0.02</td>
</tr>
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<td>PCL-C total</td>
<td>52.4 (16.3)</td>
<td>41.9 (16.8)</td>
<td>-10.5</td>
<td>&lt;0.001</td>
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<td></td>
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<tr>
<td></td>
<td>Reexperiencing</td>
<td>14.2 (5.8)</td>
<td>11.0 (5.3)</td>
<td>-3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Avoidance</td>
<td>5.7 (2.6)</td>
<td>4.8 (2.5)</td>
<td>-0.9</td>
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</tr>
<tr>
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<td>Hyperarousal</td>
<td>15.7 (5.6)</td>
<td>12.6 (5.5)</td>
<td>-3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
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<td>Hyperarousal</td>
<td>16.9 (5.2)</td>
<td>13.4 (3.3)</td>
<td>-3.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are shown as mean (SD).

Abbreviations: CPSS, Child PTSD Symptom Scale; HRV, Heart Rate Variability; LF, Low Frequency; HF, High Frequency; pNN50, the percentage of successive normal cardiac interbeat intervals greater than 50 msec; PTSD-I, Posttraumatic Stress Disorder Interview; Rx, Relaxation; RxBr, Relaxation plus Breathing; RxBrTb, Relaxation plus Breathing and Thermal Biofeedback; UPID, UCLA PTSD Index for DSM-IV; PTSD-R, PTSD Reaction Index; HTQ, Harvard Trauma Questionnaire; Re, Reexperiencing; AN, Avoidance and Numbing; Ar, Arousal; PCL-S, PTSD Checklist-Specific Version; CAPS, the Clinician Administered PTSD Scale; PCL-M, PTSD Checklist-Military Version.
FIGURE 1. Flow of systemic review process.

92 articles identified through database searching

↓

76 publications were removed after abstract screening
  26 unrelated subjects
  9 book chapters
  7 dissertations
  22 editorials, comments, or reviews
  12 unavailable full-texts

↓

16 full text articles assessed for eligibility

↓

3 articles excluded based on originality of the study

↓

13 studied included
FIGURE 2. (A) Mean scores of CAPS and PCL-M decreased after 8-week meditation. Adapted from Rosenthal et al (2011). † p = 0.02. ‡ p < 0.02. (B) Percent of participants with PTSD symptom clusters measured by Harvard Trauma Questionnaire (HTQ) after a 12-session mind-body program at baseline, post-treatment at weeks 4, and follow-up at weeks 12. Adapted from Gordon et al (2008). * p = 0.001. ** p < 0.001.
FIGURE 3. (A) Changes in PTSD symptom clusters measured by PCL-C subscale scores of veterans who participated in mindfulness-based stress reduction (MBSR). Adapted from Kearney et al (2012). (B) Scores on Child PTSD Symptom Scale (CPSS). Adapted from Staples et al (2011). * $p < 0.01$. ** $p < 0.05$. † $p < 0.001$. ‡ $p = 0.003$. 
FIGURE 4. A suggested schema for mind-body PTSD intervention modality by age group.

Subjects with PTSD

Promising Candidates for Mind-body Interventions
(Adult and older children)

Effective Mind-body Intervention
Yoga/Taichi/Qigong
Breathing/Stretching
Mindfulness-based Stress Reduction
Relaxation
Meditation
Biofeedback
Autogenic Training

Effective Interventions
Relaxation
Narrative Exposure Therapy
Drawings

Suboptimal Candidates for Mind-body Intervention
(Younger children)

Efficacy Unknown
(Older adult)

Further research required

Expected Benefits
Reduction in symptom severity
Reduction in HRV
Reduction in pain
Increased sleep patterns
Increased soothing effect
References


CHAPTER III

A RESEARCH MANUSCRIPT

This chapter presents a complete manuscript that describes this study in proposed format, which includes an abstract, introduction, procedures, results, conclusion, and reference sections. This manuscript will be submitted to the Journal of Clinical Endocrinology & Metabolism. The formatting and style guidelines of the journal were used in the manuscript.
Mindfulness-based Stretching and Deep Breathing Exercises Normalize Serum Cortisol Levels and Reverse Symptoms of PTSD: A Prospective Randomized-Controlled Trial

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Department of Health, Exercise, and Sports Sciences (S.H.K., S.M.S., L.K., C.M.), Clinical and Translational Science Center (S.H.K., C.Q., M.R.B.), and Department of Internal Medicine (M.R.B.), University of New Mexico, Albuquerque, NM 87131

ABSTRACT

Context: Cortisol, the human glucocorticoid, plays a key role in the pathophysiology of posttraumatic stress disorder (PTSD). It is known that individuals with chronic PTSD suffer from low basal cortisol levels. Endogenic normalization of basal cortisol concentration through exercise may have a therapeutic effect on treating PTSD symptoms, yet little is known about the association between exercise-induced endogenic increase of cortisol and PTSD symptom reduction. Objective: To identify whether mindfulness-based stretching and deep breathing exercise (MBX) increases basal cortisol levels, examine if MBX reduces PTSD symptom severity, and evaluate MBX as a complementary intervention for PTSD. Design: Prospective, randomized, controlled. Setting: University of New Mexico Hospital. Participants: 29 nurses with PTSD symptoms, ages 45-53, with 28 female. Intervention: 8-week bi-weekly 60-minute MBX
Main Outcome Measures: Serum cortisol and PTSD Checklist-Civilian version (PCL-C) at weeks 0, 4, 8, 12, and 16. Results: Twenty-eight participants completed the study procedures. In EX group, serum cortisol levels increased significantly from 9.6±4.1 μg/dl at baseline to 14.6±5.7 μg/dl at week 8 (p=0.0039); PTSD symptom severity decreased significantly from PCL-C scores of 43.1±11.2 at baseline to 24±3.3 at week 8 (p=0.0002); and the effects were maintained at follow-up at week 16 with cortisol concentration of 14.0±3.9 μg/dl (p= 0.5706) and PCL-C scores of 25.0±5.1 (p=0.8013). Conclusions: The results indicate a strong relationship between changes in cortisol levels and changes in PTSD symptom severity. This study provides preliminary evidence that programs aimed at reducing symptom severity in individuals with chronic PTSD should consider a mind-body intervention. To our knowledge, this is the first randomized controlled trial to assess the therapeutic benefits of MBX in individuals with PTSD symptoms using both biomarkers and PCL-C scores measuring the long-term effects of cortisol changes.

Abbreviations: PTSD, posttraumatic stress disorder; PCL-C, PTSD Checklist-Civilian version; MBX, mindfulness-based stretching and deep breathing exercise; HPA axis, hypothalamic-pituitary-adrenal axis; CRH, corticotrophin-releasing hormone; ACTH, adrenocorticotropic hormone; DHEAS, dehydroepiandrosterone-sulfate; HRV, heart rate variability; MDD, major depressive disorder.
Introduction

Posttraumatic stress disorder (PTSD) is a type of anxiety disorder that can result from exposure to a traumatic event (APA, 1987). In any given year, 7.7 million Americans over the age of 18 are diagnosed with PTSD (National Institute of Mental Health, 2011). A recent study of intensive care unit (ICU) nurses found them to be at high risk for developing PTSD as a result of repetitive exposure to extreme stressors including high patient mortality and morbidity, daily exposure to traumatic events, and the inability to adjust to extreme environments, with 24% of participating nurses testing positive for PTSD symptoms (Mealer, Shelton, Berg, Rothbaum, & Moss, 2007). In the workplace, persistent PTSD symptoms lead to reduced job satisfaction and productivity, aversion to work (Gates & Gillespie, 2008), and increased absenteeism (Laposa & Alden, 2003), compassion fatigue (Potter et al., 2010), and burnout (Acker, 1993). Considering the 17% vacancy rate for critical care nurses and a predicted 114,000 vacant critical care nursing positions in the United States by 2015, PTSD may be a significant contributor to the increasing shortage of critical care nurses (Mealer, et al., 2007).

PTSD is a debilitating disorder that is often comorbid with other diseases (Libby, 2012) such as hypertension, diabetes, metabolic syndrome, and depression. Individuals with PTSD also suffer substantial social and interpersonal problems and impaired quality of life stemming from the long-term presence of intrusive, avoidant and hyperarousal symptoms. Although pharmacological and cognitive therapy interventions have proven efficacy in the treatment of PTSD (Grodin, Piwowarczyk, Fulker, Bazazi, & Saper, 2008), residual symptoms remain problematic. Substantial evidence has shown that mind-body practices have a positive impact on quality of life, reduce stress, and improve
health outcomes among individuals with PTSD (Barnes, 2008; National Institute of Mental Health, 2011). In 2010, 39% of individuals with PTSD reported using complementary and alternative medicine (CAM) interventions, including mind-body practices that incorporate various types of stretching movements and postures with deep breathing (i.e., yoga, tai chi, and qigong) (Libby, 2012). In our study, we sought to explore the underlying neuroendocrine mechanism of these types of observed improvements in quality of life measures by examining the changes in three key stress-related biomarkers (i.e., cortisol, ACTH, DHEAS) associated with the hypothalamic-pituitary-adrenal (HPA) axis, a key area of interest in individuals with stress-related disorders.

In healthy individuals, the HPA axis functions to adapt the body to new acute stressors through a cascade of hormonal responses of secretion of corticotrophin-releasing hormone (CRH) in the hypothalamus, release of adrenocorticotropic hormone (ACTH) in the anterior pituitary gland, and secretion of glucocorticoids in the adrenal cortex (Robert M. Sapolsky, Romero, & Munck, 2000). However, chronic elevation of glucocorticoids, often coupled with genetic factors, personal traumatic history, and unhealthy lifestyle, have deleterious effects on the body (McEwen, 2002) leading to dysregulation of the HPA axis. Dysfunction of the HPA axis (Yehuda & Golier, 2009), characterized by abnormally high levels of CRH and low levels of cortisol (Fig. 1) is one of the distinct neuroendocrine profiles that differentiates PTSD from other mental illnesses (Yehuda, 2002b).

Cortisol, the human glucocorticoid, plays a key role in the pathophysiology of PTSD. In healthy individuals, an increase in basal cortisol levels is associated with
improvement in declarative memory and performance accompanied by normalized glucose metabolism in the limbic system (i.e., hippocampus, amygdala, and prefrontal cortex) (Twamley, Hami, & Stein, 2004). Patients with chronic PTSD are known to have decreased basal cortisol levels (Boscarino, 1996), though not all studies agree with this finding (Lemieux & Coe, 1995; Mason et al., 2002; Pitman & Orr, 1990), and a greater sensitivity of cortisol negative feedback inhibition in the HPA axis compared to those without PTSD (Yehuda, 2002b). In persons with chronic PTSD, basal cortisol level increases are associated with symptom improvement (Aerni et al., 2004). A recent study has shown that the administration of intravenous hydrocortisone improves working memory in combat veterans with PTSD compared with a control group without PTSD (Jenkins, Langlais, Delis, & Cohen, 1998).

We know that exercise is associated with a transient increase in plasma cortisol (Brandenberger & Follenius, 1975) and improved cognitive function (Twamley, et al., 2004) in healthy individuals. A study by Telles and colleagues (2007) showed that low-to moderate intensity mindfulness-based interventions, such as tai chi and yoga, have positive effects on PTSD symptoms (Telles, Naveen, & Dash, 2007) raising the question of whether there is an accompanying change in basal cortisol levels associated with the improvement in PTSD symptoms. There is considerable research to support the neuroprotective benefits of exercise for people with chronic stress. Moderate-intensity exercise has been shown to have neurobiological effects on chronic stress-related symptoms including improved regulation of the serotonergic system (Weicker & Struder, 2001), counteraction of degradation of the hippocampus caused by chronic stress, reduction of neurobiological sensitivity to stress, and normalization of catecholamine
levels (Chytrova, Ying, & Gomez-Pinilla, 2008; Tsatsoulis & Fountoulakis, 2006). In this study, we examined the potential for low- to moderate intensity exercise-induced endogenic normalization of basal cortisol coupled with a mindfulness component to enhance emotional regulation and cognitive function, and reduce symptom severity in individuals with PTSD.

Mindfulness is a quality of consciousness that is associated with control of attention and awareness (R. M. Sapolsky, 2004). Mindfulness-based exercise promotes a direct awareness of bodily movement, sensations, and surroundings, thus often inducing positive psychological and behavioral responses. Studies have shown that mindfulness-based exercise interventions, such as yoga, tai chi, and qigong, lead to symptom reduction in patients with PTSD (Brown & Gerbard, 2005; Grodin, et al., 2008; Telles, et al., 2007). For example, Vietnam veterans who practiced yoga for six weeks showed a significant reduction in the mean scores of the Center for Epidemiologic Studies Depression Scale (CES-D) and the 17-item Hamilton Rating Scale for Depression (HRSD-17) as well as a reduction in reported sleep disturbances, flashbacks, and anger outbursts (Brown & Gerbard, 2005).

What is less clear is the impact of exercise on the endocrinologic anomalies associated with PTSD such as reduced cortisol and abnormally high levels of CRH. It has been established that individuals with chronic PTSD suffer from low basal cortisol levels (Boscarino, 1996); that low basal cortisol levels are correlated with PTSD symptom severity (Baker et al., 1999); and that basal cortisol levels may change in relation with symptom modification (Yehuda, Bierer, et al., 2009). In healthy people, we know that immediately following exercise, cortisol levels are elevated (Brandenberger & Follenius,
and that after exercise at a lower work rate (55% VO$_{2\text{max}}$) for a longer duration (up to 3 hours), plasma cortisol concentrations rise higher than those observed at a higher work rate (80% VO$_{2\text{max}}$) for a shorter duration (within 1 hour) (Robson, Blannin, Walsh, Castell, & Gleeson, 1999). However, there is little evidence of a long-term impact of exercise on basal cortisol levels because the majority of research in this area has focused on transient changes in cortisol concentrations. To fill that gap, this study tracked changes in basal serum cortisol over a 16-week period, with 8 weeks of exercise and an 8-week follow up.

In addition to low plasma and urinary cortisol levels (Yehuda, 2003), PTSD patients also have abnormally high secretion of CRH (Baker, et al., 1999; Bremner et al., 1997; Sautter et al., 2003) but a low level of ACTH (Smith et al., 1989). CRH is secreted in the hypothalamus and inhibited by the hippocampus (Herman et al., 1989; Jacobson & Sapolsky, 1991); and abnormally high secretion of CRH is associated with PTSD symptom severity (Yehuda, 2002b). Studies have shown that chronically elevated CRH in the cerebrospinal fluid (CSF) is associated with a blunted ACTH response to CRH leading to hyposcretion of ACTH in the pituitary gland (Bremner et al., 2003; Heim, Newport, Bonsall, Miller, & Nemeroff, 2001; Smith, et al., 1989), which may decrease the secretion of cortisol in the adrenal cortex (hypocortisolaemia) (Smith, et al., 1989). On the other hand, dehydroepiandrosterone sulfate (DHEAS), a glucocorticoid antagonist secreted in the adrenal cortex, is known to have a counteracting effect against excess glucocorticoid-induced neurotoxicity in the brain and prevent excitotoxic cell death in the hippocampus (Kimonides, Khatibi, Svendsen, Sofroniew, & Herbert, 1998). Endogenic production of DHEAS is reduced by age, stress, or illnesses (Goodyer et al., 1996).
Rasmusson and colleagues reported that DHEAS may play a role in resilience to stress, protecting against the development of PTSD symptom clusters such as avoidance and hyperarousal and that there is a positive correlation between serum DHEAS/cortisol ratio and human performance under extreme stress (2004). Interestingly, Jones and Moller reported that increase in DHEAS levels may indirectly inhibit the hyperactivity of amygdala leading to reduction of PTSD symptom severity (Jones & Moller, 2011).

Johnson and colleagues found that exercise significantly elevates dehydroepiandrosterone levels (1997). Also of note, DHEAS, antiglucocorticoid secreted episodically and synchronously with glucocorticoids in response to ACTH concentrations (Rosenfeld et al., 1971), protects the brain from stressors (Kimonides, et al., 1998). Increase in DHEAS and ACTH may be associated with improvement of the brain function and PTSD symptom reduction. We therefore chose to measure plasma ACTH and serum DHEAS to examine whether there would be a relationship between exercise-induced change in PTSD symptom severity and changes in the levels of serum DHEAS and plasma ACTH as a result of exercise.

The primary question this research attempted to answer was whether the resting Ante Meridiem (AM) serum cortisol levels increase in individuals with PTSD as a result of exercise, and how a potential exercise-induced increase in basal cortisol relates to PTSD symptom reduction. Endogenic normalization of cortisol concentration through exercise may have a therapeutic effect on treating PTSD symptoms. Therefore, we sought to explore whether mindfulness-based stretching and deep breathing exercise (MBX) increases cortisol levels, examine if MBX reduces PTSD symptom severity, and evaluate MBX as a complementary intervention for PTSD. We hypothesized that an exercise-
induced reduction in PTSD symptoms would be positively associated with elevation in basal cortisol levels as a result of participating in an 8-week MBX program. To test this hypothesis, we conducted a prospective randomized controlled trial in nurses with PTSD symptoms to determine the effect of MBX-induced changes in cortisol levels on PTSD symptom severity. We also examined the ratios of cortisol/DHEAS and cortisol/ACTH to determine whether MBX would be associated with a significant change in either of these ratios.

Materials and Methods

Human Subjects and Study Protocols

Nurse volunteers were recruited from the University of New Mexico Hospital through advertisement and gave their written consent prior to enrolling in the study. Initial screening of volunteers was conducted using the PTSD Checklist Civilian version (PCL-C), a 17-item self-reported instrument with good test–retest reliability and internal consistency (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996). Inclusion criteria were a total PCL-C score of at least 28, with a score of 3 or higher on one or more individual items. Exclusion criteria included an inability to participate in the exercise program, a positive answer to any of the seven screening questions on the Physical Activity Readiness Questionnaire (PAR-Q), or current use of systemic glucocorticoid. Demographics and medical history were obtained at baseline. Changes in PTSD symptoms and fasting serum cortisol were assessed at an individually standardized time (around 8:00 AM) at weeks 0, 4, 8, 12, and 16. This decision was based on the reports from previous studies on lower morning cortisol levels in those with PTSD than in
healthy individuals (Boscarino, 1996) and negative relationship between morning cortisol and PTSD symptomology (Kellner, Baker, & Yehuda, 1997). We also obtained fasting plasma ACTH and DHEAS at pre- and postintervention at the same time. Participants were instructed to refrain from the following for 72 hours prior to the blood draw and the compliance was verified by participants’ self-reporting: drinking alcohol, taking any nonprescription drugs unless absolutely necessary, and engaging in vigorous exercise. On three occasions, participants requested rescheduling for phlebotomy because they had consumed alcohol or exercised within 72 hours prior to the scheduled blood draw.

Mind-body Intervention

A series of 16 standardized, bi-weekly 60-minute MBX classes were led by a trained instructor and conducted in a conference room of the Clinical and Translational Science Center (CTSC) of the University of New Mexico. Each class included stretching and balancing movements (see Index for exercise demonstration) combined with deep breathing. Throughout the exercise sessions, the participants were instructed to pay attention to the flow of each movement at the present moment with a focus on conscious regulation of inhalation, retention, and exhalation of the breath. Particular emphasis was given on creating inner environment of positive attitude and feeling the self as it is throughout the class. Over the course of the 8 weeks, the intensity of the exercise increased but the sequence of the movements was substantially the same. Participants were asked to practice the exercise protocol at home if they chose to and record the duration of exercise time each week in a home exercise log.
Study Design and Randomization

We conducted a 3-arm prospective randomized controlled study. Twenty-nine adults participated in the study. Of 29, 22 participants who were positively screened for PTSD symptoms were randomized by coin-flip into an 8-week course of mind-body exercise group (EX) (n=11) or a control group (CON) (n=11). Seven participants who were negatively screened for PTSD were assigned to a healthy group (BASE) to establish baseline data for cortisol, ACTH and DHEAS in this population. After being assigned to BASE group, these participants did not complete any additional PCL-C evaluations because they are not symptomatic of PTSD. Study protocol and procedures were approved by the Human Research Review Committee (HRRC), the institutional review board of the University of New Mexico. We obtained oral informed consent from participants before telephone eligibility screening. Those who were eligible provided written informed consent prior to study enrollment.

Cortisol, ACTH and DHEAS

Serum cortisol was measured using a blood draw at baseline, weeks 4, and 8 for all groups. For EX group, serum cortisol was also measured at 12-week and 16-week follow-ups. Serum DHEAS and plasma ACTH were measured using a blood drawn at baseline and week 8 for all groups with an additional follow-up measurement for EX group at week 16. This series of cortisol, DHEAS and ACTH data were used to track changes in biomarker levels over the course of the study.

PCL-C Scores
The PCL-C, a 17-item self-reported instrument, measures the 17 Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) symptoms of PTSD including intrusive recollection, flashbacks, anhedonia, estrangement from others, foreshortened future, and impaired concentration (7). In a test with a sample of individuals with a variety of traumatic experiences, the PCL instrument showed a good test–retest reliability and internal consistency (Blanchard, et al., 1996; F. Weathers, Litz, Herman, Huska, & Keane, 1993). It is used for a variety of purposes including screening and diagnosing individuals for PTSD as well as monitoring symptom change during and after intervention. Participants self-report the symptom severity by rating each item on a scale ranging from 1 (not at all) to 5 (extremely) (7). Possible scores range from 17 to 85. Inclusion criteria were set at a total score of 28, with at least one individual item scored 3 or higher. Our primary interest was in tracking the change in symptom severity in individuals with high self-reported levels of stress. Participants were considered symptomatic of PTSD if they met the inclusion criteria but were not clinically diagnosed with PTSD.

Statistical Analysis

The study was originally designed to be a repeated-measures cross-over design. However, after reviewing the outcomes there appeared to be an order effect, and thus the data had to be treated as just two groups. Data analyses were conducted on the basis of intent-to-treat. We compared the changes of outcome variables at pre- and postintervention using a two-tailed t-test. We then examined each outcome over time, measuring changes in symptom severity of PCL-C scores and cortisol levels to identify
the effects of participation in the 8-week exercise program on each variable using repeated measures of Analysis of Variance (ANOVA). We also examined potential effects of confounders and interaction with intervention by covariates including age, gender, ethnicity, education, marital status, smoking status, body mass index (BMI), and duration of nursing experience. Patient characteristic variables are summarized in Table 1. Statistical analyses were conducted using SPSS and STATA.

Results

Study participants

Of 63 screened subjects, 29 met the inclusion criteria. Of 29, 22 were enrolled in the PTSD symptomatic groups and randomized into either EX or CON group and 7 were assigned to non-PTSD symptomatic BASE group. Of 22 in the PTSD symptomatic group, 21 completed the study procedures. Seven participants in the BASE group completed the study. The one subject in the control group who did not complete the study withdrew due to family-related personal matters. One participant (9%) attended 12 classes out of 16 total classes, 6 (55%) attended 13 classes, 3 (27%) attended 14 classes, and 1 (9%) attended 16 classes. Participants in the PTSD symptomatic groups were aged 46.3±9.0 years and had mean body mass index (BMI) of 27.2±6.2 kg/m² whereas participants in non-PTSD symptomatic group were aged 44.7±16.2 years and had mean BMI of 25.5±3.2 kg/m². One participant declined to answer regarding the duration of nursing experience.

Effect of exercise on overall PTSD symptom severity
As shown in Fig. 3, 8 weeks of MBX significantly reduced self-reported PTSD symptom severity in the exercise group as measured by PCL-C (from mean PCL-C score of 43.1±11.2 to 24.3±3.3, p=0.0002). Fig. 4 graphically represents both the reductions of PCL-C scores in each subjects and the overall trends toward lower PCL-C scores from baseline (red line) through week 8 (green line) as shown by the movement of data points toward the center of the graph. The mean postintervention PCL-C score of 24.3 was below the study inclusion criteria of a score of 28. Conversely, the control group mean PCL-C scores showed no significant change in 8 weeks (from 42.6±12.7 to 41.0±16.3, p=0.6572) (Table 2). A comparison of the mean decrease for the exercise and control groups showed a significant difference in the outcomes for those who had the intervention and those who did not (p=0.009). The mean decrease in the exercise group PCL-C score was 18.82±10.6 and the mean decrease in the control group PCL-C score was 1.60±11.0 (Table 3). There was a significant group-time interaction (p = 0.02).

Effect of exercise on subtypes of PTSD symptom severity

PTSD is characterized by three subtypes of symptoms: reexperiencing, avoidance and hyperarousal. Each cluster can be evaluated separately on a subscale using a distinct subset of questions from the PCL-C questionnaire. As shown in Fig. 5, the exercise group showed a significant reduction in each of the three PCL-C subscales. Mean reexperiencing scores decreased from 2.5±0.7 to 1.4±0.3 (p=0.0003) (Fig.5a). Mean avoidance scores fell from 2.5±0.8 to 1.4±0.3 (p=0.0007) (Fig.5b). Mean hyperarousal scores decreased from 2.7±0.9 to 1.5±0.4 (p=0.0005) (Fig.5c). The control group PCL-C subscale changes were not significant, changing from 2.6±1.1 to 2.4±1.1 (p=0.5593) for
the reexperiencing cluster, from 2.5±0.6 to 2.5±0.8 (p=0.8754) for the avoidance cluster, and from 2.8±0.8 to 2.7±1.1 (p=0.9315) for the hyperarousal cluster.

At the 16-week follow-up (Table 4), the improvement in PCL-C scores was maintained. The mean PCL-C score at 16 weeks was 25.0±5.1 compared to the 8-week mean score of 24.3±3.3 (p=0.8013).

Effect of exercise on serum cortisol

Serum cortisol concentrations in the exercise group rose from 9.6±4.1 μg/dl to 14.7±5.7 μg/dl (p=0.0039) after 8 weeks of MBX (Fig. 6A and 7). The control group showed no significant change in serum cortisol concentration (12.9±6.9 μg/dl to 12.9±4.9 μg/dl, p=0.3566) at pre- and postintervention (Table 2). Comparison of cortisol levels between EX and BASE groups revealed that there was a significant difference at preintervention (9.6 μg/dl, 13.9 μg/dl, EX and BASE respectively, p = 0.0350) but there was no difference at postintervention (14.6 μg/dl, 14.8 μg/dl, EX and BASE respectively, p = 0.4893). At the 16-week follow-up, the changes in the exercise group were maintained. The mean serum cortisol at 16 weeks was 14.0±3.9 μg/dl compared to the postintervention measure of 14.7±5.7 μg/dl (p=0.5706). A comparison of the mean increase in cortisol level for both groups showed a significant difference, with the exercise group experiencing a mean increase of 5.06±4.5 μg/dl and the control experiencing a mean increase of 0.82±4.2 μg/dl (p=0.0188, Table 3).

Effect of exercise on other biomarkers

We also examined the effect of exercise on ACTH and DHEAS at postintervention. In the exercise group, there were no significant changes in levels of
ACTH (19.8 pg/ml preintervention and 22.2 pg/ml postintervention, \( p=0.1306 \)) or DHEAS (85.6 μg/dl preintervention and 94.8 μg/dl postintervention, \( p=0.1897 \)). However, the ACTH levels of the exercise group were significantly higher postintervention than in the control group (\( F (1, 19) = 6.78, p = 0.0108 \)), whereas the DHEAS levels of the exercise group showed no significant difference from the control group postintervention (\( F (1, 19) = 0.02, p = 0.8768 \)). In addition, there were significant changes in the exercise group’s cortisol/ACTH ratio (increased from 0.65 to 0.87, \( p=0.0231 \)) and cortisol/DHEAS ratio (increased from 0.15 to 0.20, \( p=0.0126 \)) (Fig. 8).

Correlation of PTSD symptoms with hormone responses

There was a significant positive correlation between the participation in the MBX intervention and the PCL-C scores in the EX group: \( r = 0.67, p = 0.001 \) (Fig. 6A), but there was no significant correlation between the change in cortisol in response to exercise and total PCL-C scores at postintervention: \( r = 0.18, p = 0.467 \) (Fig. 6B). When controlling for participation in exercise, 0.38 unit increase in cortisol is associated with a one point decrease in the PCL-C score (PCL-C 3 = - 0.38 cortisol 3 – 11.6 exercise + 44.6073, \( R^2 = 0.27 \)) (Fig. 9)

Discussion

This is the first randomized controlled trial to examine the therapeutic benefits of mindfulness-based stretching and breathing exercises in individuals with PTSD using both biomarkers and self-reported symptom severity scores. Participation in an 8-week MBX program yielded a 44% reduction in PCL-C scores and a 34% increase in serum
cortisol concentration. The effects were maintained at week 16. There were no significant differences in ages, ethnicity, education, marital status, smoking status, and nursing experience of the exercise group compared to the control group.

In a comparison of cortisol levels between the EX and BASE groups, cortisol levels in the EX group were significantly lower at preintervention ($p = 0.0350$) but there was no significant difference at postintervention ($p = 0.3639$), indicating that normalization of cortisol levels may have occurred in the exercise group as a result of the intervention. Our data demonstrate that 8-week MBX intervention which significantly increased serum cortisol levels at week 8 also resulted in a significant reduction of PTSD symptom severity.

Considering that abnormally high secretion of CRH is associated with PTSD symptom severity (Yehuda, 2002b), the MBX-induced increase of cortisol levels, via negative feedback inhibition, may have reduced CRH secretion in the hypothalamus leading to decrease in PTSD symptom severity. This finding is consistent with previous studies demonstrating that administration of cortisol after trauma reduces the likelihood of developing PTSD (Yehuda, Bierer, et al., 2009) and decreases the retrieval of fear memories (Schelling et al., 2006). However, it is not clear whether an exercise-induced endogenous increase of cortisol would be different compared to exogenously administered cortisol on the changes of PTSD symptoms.

We also analyzed the three subtypes of PTSD symptoms: reexperiencing, avoidance and hyperarousal. The exercise group showed a 44% reduction in the mean scores of reexperiencing and avoidance subscales, and a 42% decrease in mean hyperarousal subscale scores whereas there were no significant differences in the
subscale scores in the control group. Our data show that an MBX intervention has comparable effects on all three symptom clusters resulting in improvement of both clinically and neurobiologically opposing symptom characteristics: undermodulated emotional dysregulation (reexperiencing and hyperarousal subtypes) and overmodulated emotional dysregulation (avoidance and numbness) (Lanius et al., 2010). Lanius and colleagues (2010) categorized undermodulated symptoms as being mediated by failure of prefrontal inhibition of limbic regions and overmodulated symptoms as being overly controlled by midline prefrontal inhibition of the limbic regions (Lanius, et al., 2010). Our findings have significant implications for the development of comprehensive intervention for PTSD which addresses the normalization of both overmodulation and undermodulation of emotional dysregulation. Together, these data support our hypothesis that exercise-induced reduction in PTSD symptoms is positively associated with changes in cortisol levels as a result of participating in an 8-week MBX program.

Furthermore, compliance among participants in the intervention was high: all 11 participants completed the intervention attending at least 75% of the 16 classes. Anecdotally, during their 8-week participation in the intervention, many participants voluntarily reported to the instructor that they experienced improved sleep patterns, felt more resistant to stress, had improved energy levels, felt better able to control their emotions under stress, and resumed engaging in pleasurable hobbies which they had discontinued due to high levels of stress. At the end of the intervention, more than half of the participants expressed a desire to continue attending classes. Given the hurdles to compliance with current PTSD treatment options, the high levels of voluntary compliance
with the MBX intervention suggest that it may be an attractive self-care option with a high level of patient adherence.

A unique component of MBX interventions versus typical low- to moderate-intensity exercise is the inclusion of slow and deep breathing in synchronization with the exercise movements. Slow breathing is known to have a balancing effect on the autonomic nervous system via enhanced parasympathetic activation. Jerath and colleagues (2006) reported that slow and deep breathing stimulates stretch-induced inhibitory signals and hyperpolarizes currents propagated in the cells leading to synchronization of neural elements in the heart, lungs, limbic system and cortex (Jerath, Edry, Barnes, & Jerath, 2006). Cohen and colleagues (Cohen et al., 1998) stated that slow breathing enhances heart rate variability (HRV) and vagal activity, leading to reduced psycho-physiologic arousal. Although we did not examine HRV in the study, HRV can be used as an index to measure changes in the autonomic nervous system (Song et al., 2011) and is a reliable marker of vagal (parasympathetic) activity of the heart, as well as stress vulnerability (Porges, 1995). In general, increased HRV reflects decreased sympathetic regulation and stress (Dishman et al., 2000), and is associated with reduced PTSD symptom severity (Cohen, et al., 1998).

The analysis of ACTH and DHEAS at postintervention reveals that there was no significant increase in the concentrations of ACTH and DHEAS in the exercise group. However, mean ACTH levels in the EX group were significantly higher than in the CON group at 8 weeks. Additionally, the changes in the ratios of cortisol/ACTH and cortisol/DHEAS in the EX were significant. Both ratios were significantly higher at postintervention compared to
preintervention, indicating that the rate of increase in cortisol was greater than the rate of increase in ACTH or DHEAS. We speculate that this result may be an indicator of MBX-induced up-regulation of the adrenal cortex via enhanced adrenocortical sensitivity to ACTH leading to increased cortisol release. Further study is needed to understand the exact mechanism at work. Rasmusson and colleagues (2004) reported that an increase in DHEA is negatively correlated with PTSD symptom severity and DHEA to cortisol ratio is inversely related with negative mood symptoms in premenopausal women with PTSD (Rasmusson, et al., 2004). Interestingly, as seen in Figure 10, postintervention DHEAS levels were greater compared with preintervention DHEAS levels although statistically insignificant. The increase in DHEAS levels may have been associated with reduction of PTSD symptom via the mechanism of indirect inhibition of the hyperactivity of amygdala (Jones & Moller, 2011). However, our data showed no significant association between PTSD symptom severity and DHEAS levels, possibly due to the small sample size of our study and the reliance on biomarker measurement taken at one point in time.

Measurement of changes in cortisol concentrations may be important in understanding the pathogenesis of PTSD, clinical assessment of physiological responses to stress, and treatment of PTSD (Matousek, Dobkin, & Pruessner, 2010). Recent studies have shown that lifetime PTSD is associated with significantly lower cortisol levels (Yehuda, Halligan, & Bierer, 2002d) and the differences in cortisol predict or correlate with response to treatment for PTSD symptoms (Yehuda, Bierer, et al., 2009). Recent studies reported that individuals with PTSD and lower urinary cortisol levels are significantly less responsive to psychotherapy treatment (Yehuda, Bierer, et al., 2009), and the levels of cortisol predict gene expression in the HPA axis as well as the brain and
immune cell function (Yehuda, Cai, et al., 2009). Yehuda and colleagues (2009) reported that FK506-binding protein (FKBP506), a modulator of glucocorticoid receptor (GR) sensitivity, is associated with PTSD symptom severity and cortisol levels. The authors conducted genetic studies measuring plasma cortisol using radioimmunoassay and identified a role of FKBP506 in PTSD: FKBP506 expression is reduced in PTSD and is predicted by cortisol levels, particularly in those with childhood trauma and current PTSD (Yehuda, Cai, et al., 2009). The authors suggested that lower cortisol levels may contribute to the progression to chronic, treatment-resistant PTSD via attenuation of peripheral catabolism of cortisol and suppression of HPA axis responsiveness (Yehuda, Bierer, et al., 2009).

As the participants in our study were primarily female, we ad hoc considered estradiol to be an important factor in PTSD symptom manifestation. Unfortunately, we did not obtain estradiol samples due to limited study resources. This will be of interest in our future studies as recent research has elucidated the role of estradiol in modulating the HPA axis and suggested a sex-specific genetic association of pituitary adenylate cyclase-activating polypeptide (PACAP), which is a regulator of the cellular stress response, impacting fear physiology, PTSD diagnosis and symptoms in females (Kageyama & Suda, 2009; Ressler et al., 2011).

This study is limited by a small number of participants who were predominantly female nurses with PTSD symptoms; thus there may be problems with generalizability of the outcomes to males and individuals with combat-related trauma. Because the study participants were not clinically diagnosed with PTSD, there may be also issues with generalizability to patients with a diagnosed PTSD. However, given the small number of
PTSD-related studies conducted exclusively on civilian female populations, our findings may shed light on characteristics specific to a population that has received little attention to date. It should be noted that our findings are limited by the absence of inclusion of the participants’ menstrual cycle data.

In screening for study eligibility and PTSD symptom severity of the participants, we used PCL-C, a 17-item self-reported instrument, without diagnosis of PTSD. However, the PCL instrument has a good test–retest reliability and internal consistency (Blanchard, et al., 1996) with good psychometric properties (F. W. Weathers, Keane, & Davidson, 2001). The inclusion criteria were set sufficiently high to ensure that all participants in the EX and CON groups had levels of self-reported stress that were high enough to negatively impact their quality of life on a daily basis and to be PTSD symptomatic.

Additionally, since the time windows of phlebotomy were between 7:45 and 9:00 AM, there may be inaccuracy of assessing the morning surge of cortisol secretion in the 8:00 AM. Nonetheless, most of the participants’ phlebotomy times were internally consistent throughout the study. Participants were instructed to fast for 10-hours prior to phlebotomy and the resting cortisol levels were measured at least 72 hours after exercise to rule out the transient effects of exercise on cortisol levels.

In summary, in this study of human endocrine and exercise physiology we have demonstrated that after participation in an 8-week mind-body exercise intervention, participants experienced substantial increases in serum cortisol concentration with concurrent reduced PTSD symptom severity. Considering that early intervention is critical in ameliorating the development of PTSD (Descilo et al., 2010) and that PTSD
symptoms are strongly correlated with the degrees of distress immediately following the trauma (Descilo, et al., 2010), short-term mind-body interventions such as an 8-week mind-body intervention may provide a potent nonpharmacological treatment for individuals with PTSD. Long-term studies that examine the neuroendocrine responses of cortisol and CRH, using blood oxygen level-dependent (BOLD) brain imaging or an immunoassay such as YK130 CRF Elisa Kit (Gentaur, Paris, France), are warranted.

Acknowledgements

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Clinical Trial Registry Number: NCT01462045.

Disclosure Summary: None of the authors have any conflict of interest.
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<tr>
<th>Characteristics</th>
<th>Exercise group (n = 11)</th>
<th>Control group (n = 11)</th>
<th>Base group (n = 7)</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>47.6 (7.7)</td>
<td>45.0 (10.0)</td>
<td>44.6 (16.2)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>10 (91)</td>
<td>11 (100)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Smoking status</td>
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<tr>
<td>Ever smoked</td>
<td>5 (45)</td>
<td>4 (36)</td>
<td>1 (14)</td>
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<tr>
<td>Never smoked</td>
<td>6 (55)</td>
<td>7 (64)</td>
<td>6 (86)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.9 (5.1)</td>
<td>27.4 (7.3)</td>
<td>25.5 (3.2)</td>
</tr>
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<td>Ethnic origin</td>
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<td>African</td>
<td>1 (9)</td>
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<td>1 (14)</td>
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<tr>
<td>American Indian</td>
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<td>1 (9)</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>4 (36)</td>
<td>3 (27)</td>
<td>4 (57)</td>
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<tr>
<td>White (Not Hispanic or Latino)</td>
<td>6 (55)</td>
<td>7 (64)</td>
<td>2 (29)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>College degree</td>
<td>9 (82)</td>
<td>9 (82)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>Graduate degree</td>
<td>2 (18)</td>
<td>2 (18)</td>
<td>3 (43)</td>
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<tr>
<td>Marital status</td>
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<tr>
<td>Ever married</td>
<td>8 (73)</td>
<td>8 (73)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>Never married</td>
<td>3 (27)</td>
<td>3 (27)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>Nursing experience</td>
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<tr>
<td>Less than 5 yrs</td>
<td>3 (27)</td>
<td>2 (18)</td>
<td>2 (33)</td>
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<td>6-10 yrs</td>
<td>2 (18)</td>
<td>1 (17)</td>
<td>1 (17)</td>
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<td>11-15 yrs</td>
<td></td>
<td>1 (17)</td>
<td></td>
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<tr>
<td>More than 15 yrs</td>
<td>8 (73)</td>
<td>7 (64)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Baseline outcomes</td>
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<td></td>
</tr>
<tr>
<td>PCL-C score</td>
<td>43.1 (11.2)</td>
<td>42.4 (12.1)</td>
<td>21.8 (3.4)</td>
</tr>
<tr>
<td>Cortisol (μg/dl)</td>
<td>9.6 (4.1)</td>
<td>13.2 (6.6)</td>
<td>13.9 (5.8)</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>19.8 (10.8)</td>
<td>12.4 (4.6)</td>
<td>14.8 (5.4)</td>
</tr>
<tr>
<td>DHEAS (μg/dl)</td>
<td>85.6 (33.7)</td>
<td>91.1 (66.2)</td>
<td>90.6 (66.0)</td>
</tr>
</tbody>
</table>

† Data are means (SD) or numbers (%).
†† One participant declined to answer about the length of nursing experience.
### TABLE 2. Summary results of PCL-C scores and Cortisol at Pre- and Postintervention.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Exercise group (n=11)</th>
<th>Control group (n=11)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Wk 8</td>
<td></td>
</tr>
<tr>
<td>PCL-C total</td>
<td>43.1 (11.2)</td>
<td>24.3 (3.3)</td>
<td>0.0002***</td>
</tr>
<tr>
<td>PCL-C subscales</td>
<td></td>
<td></td>
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<tr>
<td>Reexperiencing</td>
<td>2.5 (0.7)</td>
<td>1.4 (0.3)</td>
<td>0.0003***</td>
</tr>
<tr>
<td>Avoidance</td>
<td>2.5 (0.8)</td>
<td>1.4 (0.3)</td>
<td>0.0008***</td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>2.7 (0.9)</td>
<td>1.5 (0.4)</td>
<td>0.0005***</td>
</tr>
<tr>
<td>Cortisol</td>
<td>9.6 (4.1)</td>
<td>14.6 (5.7)</td>
<td>0.0039**</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
<td>Wk 8</td>
<td></td>
</tr>
<tr>
<td>PCL-C total</td>
<td>42.6 (12.7)</td>
<td>41.0 (16.3)</td>
<td>0.6572</td>
</tr>
<tr>
<td>PCL-C subscales</td>
<td></td>
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<td></td>
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<tr>
<td>Reexperiencing</td>
<td>2.6 (1.1)</td>
<td>2.4 (1.1)</td>
<td>0.5593</td>
</tr>
<tr>
<td>Avoidance</td>
<td>2.5 (0.6)</td>
<td>2.5 (0.8)</td>
<td>0.8754</td>
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<tr>
<td>Hyperarousal</td>
<td>2.8 (0.8)</td>
<td>2.7 (1.1)</td>
<td>0.9315</td>
</tr>
</tbody>
</table>

\(^a\) Data are means (SD). SD, standard deviation. Unit of cortisol = \(\mu\)m/dl. p-values are for two-sided \(t\)-test. Starred values are significant at the ***0.1 percent and **1 percent levels.

### TABLE 3. Comparison of the change in mean PCL-C scores and cortisol levels for Exercise and Control Groups.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Exercise Group</th>
<th>Control Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL-C mean decrease</td>
<td>18.82 (10.6)</td>
<td>1.60 (11.0)</td>
<td>0.0009***</td>
</tr>
<tr>
<td>Cortisol mean increase</td>
<td>5.06 (4.5)</td>
<td>0.82 (4.2)</td>
<td>0.0188*</td>
</tr>
</tbody>
</table>

\(^a\) Data are means (SD). SD, standard deviation. Unit of cortisol = \(\mu\)m/dl. p-values are for two-sided \(t\)-test. Starred values are significant at the ***0.1 percent and *5 percent levels.

### TABLE 4. Summary results of follow-up PCL-C scores and Cortisol values for exercise group.\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Exercise Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 8</td>
<td>24.3 (3.3)</td>
<td>0.8013</td>
</tr>
<tr>
<td>Wk 16</td>
<td>25.0 (5.1)</td>
<td></td>
</tr>
<tr>
<td>PCL-C total</td>
<td>25.0 (5.1)</td>
<td></td>
</tr>
<tr>
<td>PCL-C subscales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reexperiencing</td>
<td>1.4 (0.3)</td>
<td>0.6783</td>
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<tr>
<td>Avoidance</td>
<td>1.4 (0.3)</td>
<td>0.4269</td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>1.5 (0.4)</td>
<td>0.7517</td>
</tr>
<tr>
<td>Cortisol</td>
<td>14.6 (5.7)</td>
<td>0.5706</td>
</tr>
</tbody>
</table>

\(^a\) Data are means (SD). Unit of cortisol = \(\mu\)m/dl. Values are in mean (SD). p-values are for two-sided \(t\)-test.
FIG. 1. Schematic illustration of HPA axis regulation. CRH in the hypothalamus is released to the anterior pituitary gland stimulating ACTH secretion, which stimulates the adrenal cortex, triggering glucocorticoids (human cortisol) release. Cortisol regulates CRH and ACTH secretion via a negative feedback inhibition loop. In individuals with PTSD, due to the hypersensitized feedback inhibition, cortisol levels are abnormally lower and CRH levels are higher compared to individuals without PTSD.

Abbreviation: HPA, hypothalamic-pituitary-adrenal; CRH, corticotrophin-releasing hormone; ACTH, adrenocorticotropic hormone; PTSD, posttraumatic stress disorder.
Fig. 2. Participant flow diagram.
FIG. 3. PCL-C scores measured at baseline, week 4 and week 8.

FIG. 4. Changes in PCL-C scores by subject. Spoke numbers 1-11 correspond to exercise group subject numbers: n=11. PCL-C scores ranging from 17 to 70 are shown in the 0-70 scale.
FIG. 5. Changes in PTSD subtypes in exercise group measured at baseline, weeks 4 and 8. A, reexperiencing; B, avoidance; and C, hyperarousal.
FIG. 6. A. Changes in PCL-C scores and serum cortisol (µg/dl) at pre- and postintervention in exercise group. B. Changes in PCL-C scores and serum cortisol (µg/dl) at pre- and postintervention in control group.
FIG. 7. Changes in cortisol levels by subject. Spoke numbers 1-11 correspond to exercise group subject numbers: n=11. Cortisol levels ranging from 5 to 30 \( \mu g/dl \) are shown in the 0-30 scale.

FIG. 8. Ratios of Cortisol/ACTH and Cortisol/DHEAS at baseline and week 8.
FIG. 9. Correlations between changes in PCL-C score and cortisol concentration (µg/dl) at postintervention. \( R^2 = 0.27, \ p = 0.437 \).

FIG. 10. Changes in DHEAS concentration (µg/dl) in participants in exercise group at pre- and postintervention. DHEAS: dehydroepiandrosterone sulfate.
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CHAPTER IV: SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Summary

Cortisol plays a key role in the pathophysiology of PTSD. Individuals with chronic PTSD suffer from low basal cortisol levels and research have shown therapeutic potential of increased cortisol on treating PTSD symptoms. We conducted a prospective randomized control trial to identify whether mindfulness-based stretching and deep breathing exercise would increase basal cortisol levels and lead to reduction of PTSD symptom severity. The followings are our hypotheses and findings:

1. **Nurses who are positively screened for PTSD and participate in an 8-week mindfulness-based stretching and breathing exercises would have greater changes in cortisol levels compared to the control group.**

   Our results showed that there was a significant difference in the changes in basal serum cortisol levels in the exercise group compared to the changes in basal serum cortisol levels in the control group.

2. **Nurses who are positively screened for PTSD and participate in an 8-week mindfulness-based stretching and breathing exercises would have greater changes in PTSD symptom severity compared to the control group.**

   Our data showed that there was a statistically and clinically significant difference in the changes in PTSD symptom severity in the exercise group measured using PCL-C instrument compared to the changes in PTSD symptom severity in the control group.

3. **There would be a positive association between exercise-induced reduction in**
PTSD symptom severity and changes in cortisol levels as a result of participating in an 8-week mindfulness-based stretching and breathing exercises.

There was a significant positive correlation between the participation in the mindfulness-based stretching and breathing exercise intervention and the PCL-C scores in the exercise group, however, there was no significant correlation between the change in cortisol in response to exercise and total PCL-C scores at postintervention. Future research with larger sample size and cortisol collections at multiple time points may produce different results.

In summary, we have demonstrated that substantial increases in mind-body exercise-induced serum cortisol concentration were concurrent with reduced PTSD symptom severity.

**Limitations**

This study was conducted with a small number of participants of predominantly female nurses with PTSD symptoms. Thus the results of the study may not be generalizable to males and combat veterans.

**Conclusions and Applications**

Our data demonstrates that short-term mindfulness-based stretching and deep breathing exercises significantly improves cortisol levels and symptom severity in individuals with PTSD. Therefore, a program that integrated mind-body exercise may be an effective nonpharmacologic complementary program for treatment of PTSD.
Recommendation

Future research should investigate the effect of mind-body exercise-induced increase in basal cortisol levels on hypothalamic CRH secretion using brain imaging technology. Further, brain imaging studies may enhance our understanding of the relationship between the mind-body exercise-induced changes in the dynamics of the HPA axis and the structural and functional changes in the prefrontal cortex, hippocampus and amygdala. It would be also interesting to examine the roles of sex-specific genetic biomarkers and discover individualized gender-specific treatments.
The University of New Mexico Health Sciences Center
Consent to Participate in Research

The efficacy of mindfulness-based stretching and breathing exercise as a complementary therapy for posttraumatic stress disorder: A Prospective Randomized Study

Purpose and General Information
You are being asked to participate in a research study that is being done by Mark R. Burge, MD, who is the Principal Investigator, and his associates. This research is being done to evaluate the relationship between exercise-induced reduction in symptoms of stress and exercise-induced changes in cortisol levels. You are being asked to participate because you are working as a nurse at UNM Hospital and you have met the study screening criteria. Approximately 33 people will take part in this study at the University of New Mexico. The CTSC is funding this study.

This form will explain the study to you, including the possible risks as well as the possible benefits of participating. This is so you can make an informed choice about whether or not to participate in this study. Please read this Consent Form carefully. Ask the investigators or study staff to explain any words or information that you do not clearly understand.

It will take approximately 15 minutes to complete this form.

What will happen if I participate?
If you agree to be in this study, you will be asked to read and sign this Consent Form. After you sign the Consent Form, the following things will happen:

You will be assigned by chance (like a flip of a coin) to either a CONTROL group or EXERCISE group. If you are assigned to a CONTROL group, don't worry, you will participate in exercise during the second 8-week session. The total length of the study is 16 weeks, including an 8-week exercise portion and an 8-week non-exercise portion. Prior to beginning the study, you will be asked to fill out a survey and will have blood drawn. During the 8-week exercise portion of the study, you will be asked to attend a 60-minute exercise class twice a week for 8 weeks, you may be asked to fill out a survey twice and will have blood drawn twice. During the 8-week non-exercise portion of the study, you may be asked to fill out a survey twice and will have blood drawn twice. The exercise sessions will consist of 10-minute warm-up with low- to moderate-intensity breathing and conditioning exercises, 40-minute low- to moderate-intensity mindfulness-based movement exercise, and 10-minute cool-down. The control condition will consist of doing the activities you normally do. The instructor of the exercise program will not know the details of your self-reported stress symptoms as your identity is coded to protect your privacy. However, this information is available to the principal investigator of the study (PI), and the study coordinator.

You will be asked questions regarding your medical history, current medical conditions including medications, recent alcohol use including problems associated with alcohol and specific problems related to illegal drug use or abuse of prescription drugs.
You will be asked to complete a Physical Activity Readiness Questionnaire (PAR-Q) to be sure you can safely participate in the exercise program.
You will be asked to complete a questionnaire that asks about your feelings (such as 'Do you feel depressed today?') You may refuse to answer any questions at any time. These questionnaires will take about 30 minutes to complete.

A maximum of eleven mL of blood will be drawn with a needle from a vein in your arm at each blood draw for laboratory testing to check your cortisol, adrenocorticotropic hormone (ACTH), and Dehydroepiandrosterone-sulfate (DHEA-S) levels.

The blood collected for this research study will be sent to a central laboratory (TriCore, Albuquerque, NM). Your name and medical record number will be removed from the sample and labeled with a unique code number before being shipped.

Participation in this study will take a total of approximately 20 hours over a period of 16 weeks.

**What are the possible risks or discomforts of being in this study?**

Every effort will be made to protect the information you give us. However, there is a small risk of loss of confidentiality that may result in stigmatization or hardship.

Other risks and side effects are listed below:

- Blood drawing risks: Drawing blood may cause temporary pain and discomfort from the needle stick, occasional bruising, sweating, feeling faint or lightheaded and in rare cases infection.
- There are risks of stress, emotional distress, inconvenience and possible loss of privacy and confidentiality associated with participating in a research study.
- Exercise risks include: musculoskeletal injury. During exercise, you may experience fatigue, nausea, dizziness, fainting, breathlessness, or dyspnea, or psychological stress. Low- to moderate-intensity exercise has a very low risk of death or heart attack.

**How will my information be kept confidential?**

Your name and other identifying information will be maintained in locked files, available only to authorized members of the research team, for the duration of the study. For any information entered into a computer, the only identifier will be a unique study identification (ID) number. All written questionnaires completed by you will be coded with a unique identifying number and will never be stored together with identifiable information to minimize the risk to loss of confidentiality. Any personal identifying information and any record linking that information to study ID numbers will be destroyed when the study is completed. Information resulting from this study will be used for research purposes and may be published; however, you will not be identified by name in any publications.

Information from your participation in this study may be reviewed by federal and state regulatory agencies, and by the UNM Human Research Review Committee (HRRC) which provides regulatory and ethical oversight of human research.

To help us further protect the confidentiality of your data, the investigators have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, we cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure of coded data (your name will not be on it) will be necessary, however, upon request of DHHS (Dept. of Health and Human Services) or other federal agencies for audit or evaluation purposes.
You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note, however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate to withhold this information. This means that you and your family must also actively protect your own privacy and the confidentiality of your data. Finally, you should understand that if the investigators learn about abuse of a child or elderly person or that you intend to harm yourself or someone else, we will report that information to the proper authorities.

What are the benefits to being in this study?
There may or may not be direct benefit to you from being in this study. However, your participation may help find out how treatment for people who suffer from severe stress symptoms can be improved. The exercise program is noncompetitive, self-paced, low- to moderate-intensity physical stretching, movement and breathing. Rhythmic movements that are coordinated with breathing may help you experience a sense of inner calm, improved self-regulation, and reduced feelings of stress. Additionally, the physical exercises may lead to improved physical fitness including increased muscle tone, flexibility, balance, and cardiopulmonary capacity.

What other choices do I have if I don’t participate?
Taking part in this study is voluntary so you can choose not to participate.

Will I be paid for taking part in this study?
In return for your time and the inconvenience of participating in this study, you will be paid $20 for the participation in the first 8-week portion of the study, and additional $30 for the participation in the second 8-week portion of the study. You will receive each stipend approximately (3) weeks after completion of each 8-week portion of the study.

Can I stop being in the study once I begin?
Yes. You can withdraw from this study at any time without affecting your access to care.

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, if you do not follow study procedures, or if it is in your best interest or the study’s best interest to stop your participation.

Authorization for Use of Your Protected Health Information (HIPAA)
As part of this study, we will be collecting health information about you. This information is “protected” because it is identifiable or “linked” to you.

Protected Health Information (PHI)
By signing this Consent Document, you are allowing the investigators and other authorized personnel to use your protected health information for the purposes of this study. This information may include: medical history, body mass index, blood cortisol, ACTH, and DHEA-S levels, results of screening questionnaires and information about ongoing mental health treatment.

In addition to researchers and staff at UNMHSC and other groups listed in this form, there is a chance that your health information may be shared (re-disclosed) outside of the research study and no longer be protected by federal privacy laws. Examples of this include disclosures for law enforcement, judicial proceeding, health oversight activities and public health measures.
Right to Withdraw Your Authorization
Your authorization for the use of your health information for this study shall not expire unless you cancel this authorization. Your health information will be used as long as it is needed for this study. However, you may withdraw your authorization at any time provided you notify the UNM investigators in writing. To do this, please send a HIPAA Research Withdrawal Form or letter notifying them of your withdrawal to:
Mark R. Burge, MD
MSC 10-5550
1 University of New Mexico
Albuquerque New Mexico 87131

Please be aware that the research team will not be required to destroy or retrieve any of your health information that has already been used or shared before your withdrawal is received.

Refusal to Sign
If you choose not to sign this consent form and authorization for the use of your PHI, you will not be allowed to take part in the research study.

What if I have questions or complaints about this study?
If you have any questions, concerns or complaints at any time about the research study, Mark R. Burge, MD, or his associates will be glad to answer them at 505-272-0280 during regular business hours. If you need to contact someone after business hours or on weekends, please call Sang Kim at 505-795-4545. If you would like to speak with someone other than the research team, you may call the Human Research Review Committee (HRRC) at (505) 272-1129. The HRRC is a group of people from UNM and the community who provide independent oversight of safety and ethical issues related to research involving human subjects.

What are my rights as a research subject?
If you have questions regarding your rights as a research subject, you may call the HRRC at (505) 272-1129 or visit the HRRC website at http://hsc.unm.edu/som/research/hrrc/.

Consent and Authorization
You are making a decision whether to participate in this study. Your signature below indicates that you read the information provided (or the information was read to you). By signing this Consent Form, you are not waiving any of your legal rights as a research subject.

I have had an opportunity to ask questions and all questions have been answered to my satisfaction. By signing this Consent Form, I agree to participate in this study and give permission for my health information to be used or disclosed as described in this Consent Form. A copy of this Consent Form will be provided to me.

Name of Adult Participant (print)  Signature of Adult Participant  Date

I have explained the research to the subject and answered all of his/her questions. I believe that he/she understands the information in this consent form and freely consents to participate.

Name of Research Team Member  Signature of Research Team Member/Date
1/30/2012

University of New Mexico Health Sciences Center
Dr. Mark R. Burge
UNM Clinical and Translational Science Center
1 University of New Mexico
MSC08 4635
Albuquerque, NM 87131

Dear Dr. Burge,

Enclosed is the Confidentiality Certificate protecting the identity of research subjects in your project entitled, 'The Efficacy of Mindfulness-Based Stretching and Breathing Exercise as a Complementary Therapy for Posttraumatic Stress Disorder: A Prospective Randomized Study'. Please note that the Certificate expires on 09/30/2012.

Please be sure that the consent form given to research participants accurately states the intended uses of personally identifiable information (including matters subject to reporting) and the confidentiality protections, including the protection provided by the Certificate of Confidentiality with its limits and exceptions.

If you determine that the research project will not be completed by the expiration date, 09/30/2012, you must submit a written request for an extension of the Certificate three months prior to the expiration date. If you make any changes to the protocol for this study, you should contact me regarding modification of this Certificate. Any requests for modifications of this Certificate must include the reason for the request, documentation of the most recent IRB approval, and the expected date for completion of the research project.

Please advise me of any situation in which the Certificate is employed to resist disclosure of information in legal proceedings. Should attorneys for the project wish to discuss the use of the Certificate, they may contact the Office of the NIH Legal Advisor, National Institutes of Health, at (301) 496-6043.

Correspondence should be sent to:

Donna Jones
CoC Coordinator
National Center for Advancing Translational Sciences
6701 Rockledge Drive, Room 9171
Bethesda, MD 20892
Telephone: (301) 594-4734
Fax: (301) 480-5848

Sincerely,

[Signature]
Donna Jones
CERTIFICATE OF CONFIDENTIALITY
CC-RR-12-03
issued to
University of New Mexico Health Sciences Center
conducting research known as
The Efficacy of Mindfulness-Based Stretching and Breathing Exercise as a Complementary Therapy for Posttraumatic Stress Disorder: A Prospective Randomized Study

In accordance with the provisions of section 301(d) of the Public Health Service Act 42 U.S.C. 241(d), this Certificate is issued in response to the request of the Principal Investigator, Dr. Mark R. Burge, to protect the privacy of research subjects by withholding their identities from all persons not connected with this research. Dr. Burge is primarily responsible for the conduct of this research, which is supported by the National Center for Advancing Translational Sciences aka NCRR grant number UL1 RR031977.

Under the authority vested in the Secretary of Health and Human Services by section 301(d), all persons who:
1. are enrolled in, employed by, or associated with the University of New Mexico Health Sciences Center and their contractors or cooperating agencies and
2. have in the course of their employment or association access to information that would identify individuals who are the subjects of the research pertaining to the project known as The Efficacy of Mindfulness-Based Stretching and Breathing Exercise as a Complementary Therapy for Posttraumatic Stress Disorder: A Prospective Randomized Study

are hereby authorized to protect the privacy of the individuals who are the subjects of that research by withholding their names and other identifying characteristics from all persons not connected with the conduct of that research.

The aim of this research project is to examine the relationship between exercise-induced Post Traumatic Stress Disorder (PTSD) symptom reduction and exercise-induced changes in stress-related biomarkers (i.e., cortisol, ACTH, and DHEA-S) levels using a prospective crossover randomized clinical trial design.

A Certificate of Confidentiality is needed because sensitive information will be collected during the course of the study. The certificate will help researchers avoid involuntary disclosure that could expose subjects or their families to adverse economic, legal, psychological and social consequences.

All subjects will be assigned a code number and identifying information and records will be kept in locked files at the Institution.

This research is currently underway and is expected to end on 09/30/2012.

As provided in section 301 (d) of the Public Health Service Act 42 U.S.C. 241(d):

'Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.'

This Certificate does not protect you from being compelled to make disclosures that: (1) have been consented to in writing by the research subject or the subject's legally authorized representative; (2) are required by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) or regulations issued under that Act; or (3) have been requested from a research project funded by the National Institutes of Health (NIH) or the Department of Health and Human Services (DHHS) by authorized representatives of those agencies for the purpose of audit or program review.
CERTIFICATE OF CONFIDENTIALITY
CC-RR-12-03
issued to
University of New Mexico Health Sciences Center
conducting research known as
The Efficacy of Mindfulness-Based Stretching and Breathing Exercise as a Complementary Therapy for Posttraumatic Stress Disorder: A Prospective Randomized Study

This Certificate does not represent an endorsement of the research project by the DHHS. This Certificate is now in effect and will expire on 09/30/2012. The protection afforded by this Confidentiality Certificate is permanent with respect to subjects who participate in the research during the time the Certificate is in effect.

Date: 1/30/2012

Kathy L Hudson, Ph.D.
Deputy Director for Science, Outreach, and Policy National Institutes of Health, Acting Deputy Director
National Center for Advancing Translational Sciences
Demographic Questionnaire

Your Name ________________________         Your Height ____________     Your Weight ____________

How would you classify yourself?
  ○ White(Not Hispanic or Latino)
  ○ Hispanic or Latino (All Races)
  ○ African-American
  ○ American Indian
  ○ Asian
  ○ Pacific Islander

What is the highest level of education you have completed?
  ○ Less than college degree
  ○ College degree
  ○ Graduate school

What is your current marital status?
  ○ Single
  ○ Married
  ○ Divorced
  ○ Widowed

How is your smoking status?
  ○ Current smoker
  ○ Smoked in the past
  ○ Never smoked

How long have you been working as a nurse in the ICU?
  ○ Less than 2 years
  ○ 2-5 years
  ○ 6-10 years
  ○ 11-15 years
  ○ More than 15 years
Medical History Questionnaire

Demographic Information

<table>
<thead>
<tr>
<th>Last name</th>
<th>First name</th>
<th>Middle initial</th>
</tr>
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<tbody>
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<tr>
<th>Date of birth</th>
<th>Sex</th>
<th>Home phone</th>
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<thead>
<tr>
<th>Address</th>
<th>City, State</th>
<th>Zip code</th>
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<th>Work phone</th>
<th>Family physician</th>
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Section A

1. When was the last time you had a physical examination?

2. If you are allergic to any medications, foods, or other substances, please name them.

3. If you have been told that you have any chronic or serious illnesses, please list them.

4. Give the following information pertaining to the last 3 times you have been hospitalized.
   Note: Women, do not list normal pregnancies.

<table>
<thead>
<tr>
<th>Hospitalization 1</th>
<th>Hospitalization 2</th>
<th>Hospitalization 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for hospitalization</td>
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<tr>
<td>Month and year of hospitalization</td>
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<tr>
<td>Hospital</td>
<td></td>
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<tr>
<td>City and state</td>
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Section B

During the past 12 months

1. Has a physician prescribed any form of medication for you? □ Yes □ No
2. Has your weight fluctuated more than a few pounds? □ Yes □ No
3. Did you attempt to bring about this weight change through diet or exercise? □ Yes □ No
4. Have you experienced any faintness, light-headedness, or blackouts? □ Yes □ No
5. Have you occasionally had trouble sleeping? □ Yes □ No
6. Have you experienced any blurred vision? □ Yes □ No
7. Have you had any severe headaches? □ Yes □ No
8. Have you experienced chronic morning cough? □ Yes □ No
9. Have you experienced any temporary change in your speech pattern, such as slurring or loss of speech? □ Yes □ No
10. Have you felt unusually nervous or anxious for no apparent reason? □ Yes □ No
11. Have you experienced unusual heartbeats such as skipped beats or palpitations? □ Yes □ No
12. Have you experienced periods in which your heart felt as though it were racing for no apparent reason? □ Yes □ No

APPENDIX A.2
At present

1. Do you experience shortness or loss of breath while walking with others your own age? □ Yes □ No
2. Do you experience sudden tingling, numbness, or loss of feeling in your arms, hands, legs, feet, or face? □ Yes □ No
3. Have you ever noticed that your hands or feet sometimes feel cooler than other parts of your body? □ Yes □ No
4. Do you experience swelling of your feet and ankles? □ Yes □ No
5. Do you get pains or cramps in your legs? □ Yes □ No
6. Do you experience any pain or discomfort in your chest? □ Yes □ No
7. Do you experience any pressure or heaviness in your chest? □ Yes □ No
8. Have you ever been told that your blood pressure was abnormal? □ Yes □ No
9. Have you ever been told that your serum cholesterol or triglyceride level was high? □ Yes □ No
10. Do you have diabetes? □ Yes □ No
   If yes, how is it controlled?
   □ Dietary means □ Insulin injection
   □ Oral medication □ Uncontrolled
11. How often would you characterize your stress level as being high? □ Occasionally □ Frequently □ Constantly
12. Have you ever been told that you have any of the following illnesses? □ Yes □ No
   □ Myocardial infarction □ Arteriosclerosis □ Heart disease □ Thyroid disease
   □ Coronary thrombosis □ Rheumatic heart □ Heart attack □ Heart valve disease
   □ Coronary occlusion □ Heart failure □ Heart murmer □ Aneurysm
   □ Heart block □ Angina
13. Have you ever had any of the following medical procedures? □ Yes □ No
   □ Heart surgery □ Pacemaker implant
   □ Cardiac catheterization □ Defibrilator
   □ Coronary angioplasty □ Heart transplantation

Section C
Has any member of your immediate family been treated for or suspected to have had any of these conditions? Please identify their relationship to you (father, mother, sister, brother, etc.).

A. Diabetes

B. Heart disease

C. Stroke

D. High blood pressure

APPENDIX A.2
Par-Q & You

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the Par-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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If you answered YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the Par-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.

- Find out which community programs are safe and helpful for you.

If you answered NO honestly to all Par-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.

- take part in a fitness appraisal — this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

Informed Use of the Par-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the Par-Q but only if you use the entire form.

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

NAME ________________________________________________________________________

SIGNATURE _______________________________________________________________________________            DATE______________________________________________________

SIGNATURE OF PARENT _______________________________________________________________________            WITNESS ___________________________________________________

or GUARDIAN (for participants under the age of majority)

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Supported by: Santé Canada

98 Health Canada

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continued on other side...
Instructions: Below is a list of problems and complaints that people sometimes have in response to stressful life experiences. Please read each one carefully, put an “X” in the box to indicate how much you have been bothered by that problem in the last month.

<table>
<thead>
<tr>
<th>NO.</th>
<th>Response</th>
<th>Not at all (1)</th>
<th>A little bit (2)</th>
<th>Moderately (3)</th>
<th>Quite a bit (4)</th>
<th>Extremely (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Repeated, disturbing memories, thoughts, or images of a stressful experience from the past?</td>
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<tr>
<td>2.</td>
<td>Repeated, disturbing dreams of a stressful experience from the past?</td>
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<tr>
<td>3.</td>
<td>Suddenly acting or feeling as if a stressful experience were happening again (as if you were reliving it)?</td>
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<td>4.</td>
<td>Feeling very upset when something reminded you of a stressful experience from the past?</td>
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<td>5.</td>
<td>Having physical reactions (e.g., heart pounding, trouble breathing, or sweating) when something reminded you of a stressful experience from the past?</td>
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<td>6.</td>
<td>Avoid thinking about or talking about a stressful experience from the past or avoid having feelings related to it?</td>
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<td>7.</td>
<td>Avoid activities or situations because they remind you of a stressful experience from the past?</td>
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<tr>
<td>8.</td>
<td>Trouble remembering important parts of a stressful experience from the past?</td>
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<td>9.</td>
<td>Loss of interest in things that you used to enjoy?</td>
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<td>10.</td>
<td>Feeling distant or cut off from other people?</td>
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<tr>
<td>11.</td>
<td>Feeling emotionally numb or being unable to have loving feelings for those close to you?</td>
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<tr>
<td>12.</td>
<td>Feeling as if your future will somehow be cut short?</td>
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<td>13.</td>
<td>Trouble falling or staying asleep?</td>
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<td>14.</td>
<td>Feeling irritable or having angry outbursts?</td>
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<td>15.</td>
<td>Having difficulty concentrating?</td>
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<tr>
<td>16.</td>
<td>Being “super alert” or watchful on guard?</td>
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<td>17.</td>
<td>Feeling jumpy or easily startled?</td>
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</table>

PCL-C for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane
Please circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?

| NEVER | MONTHLY OR LESS | TWO TO FOUR TIMES A MONTH | TWO TO THREE TIMES A WEEK | FOUR OR MORE TIMES A WEEK |

NOTE: For answering these questions, one drink® is equal to 10 ounces of beer, or 4 ounces of wine, or 1 ounce of liquor

2. How many drinks containing alcohol do you have on a typical day when you are drinking?

| 1 OR 2 | 2 OR 4 | 5 OR 6 | 7 TO 9 | 10 OR MORE |

3. How often do you have six or more drinks on one occasion?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

4. How often during the last year have you found that you were not able to stop drinking once you had started?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

5. How often during the last year have you failed to do what was normally expected from you because of drinking?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

7. How often during the last year have you had a feeling of guilt or remorse after drinking?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

8. How often during the last year have you been unable to remember what happened the night before because you had been drinking?

| NEVER | LESS THAN MONTHLY | MONTHLY | WEEKLY | DAILY OR ALMOST DAILY |

9. Have you or someone else been injured as a result of your drinking?

| NEVER | YES, BUT NOT IN THE LAST YEAR | YES, DURING THE LAST YEAR |

10. Has a relative or friend, or a doctor or other health worker been concerned about your drinking or suggested you cut down?

| NEVER | YES, BUT NOT IN | YES, DURING |
Here are a few questions about drugs. Please answer as correctly and honestly as possible by indicating which answer is right for you.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Less often than once a month</th>
<th>Every month</th>
<th>Every week</th>
<th>Daily or almost every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do you use drugs other than alcohol? (See list of drugs on back side.)</td>
<td></td>
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</tr>
<tr>
<td>2. Do you use more than one type of drug on the same occasion?</td>
<td>Never</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3. How many times do you take drugs on a typical day when you use drugs?</td>
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<tr>
<td>4. How often are you influenced heavily by drugs?</td>
<td>Never</td>
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</tr>
<tr>
<td>5. Over the past year, have you felt that your longing for drugs was so strong that you could not resist it?</td>
<td>Never</td>
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</tr>
<tr>
<td>6. Has it happened, over the past year, that you have not been able to stop taking drugs once you started?</td>
<td>Never</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>7. How often over the past year have you taken drugs and then neglected to do something you should have done?</td>
<td>Never</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. How often over the past year have you needed to take a drug the morning after heavy drug use the day before?</td>
<td>Never</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. How often over the past year have you had guilt feelings or a bad conscience because you used drugs?</td>
<td>Never</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Have you or anyone else been hurt (mentally or physically) because you used drugs?</td>
<td>No</td>
<td>Yes, but not over the past year</td>
<td>Yes, over the past year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Has a relative or a friend, a doctor or a nurse, or anyone else, been worried about your drug use or said to you that you should stop using drugs?</td>
<td>No</td>
<td>Yes, but not over the past year</td>
<td>Yes, over the past year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
LIST OF DRUGS
(Note! Not alcohol!)

<table>
<thead>
<tr>
<th>Cannabis</th>
<th>Amphetamines</th>
<th>Cocaine</th>
<th>Opiates</th>
<th>Hallucinogens</th>
<th>Solvents/inhalants</th>
<th>GHB and others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marijuana</td>
<td>Methamphetamine</td>
<td>Crack</td>
<td>Smoked heroin</td>
<td>Ecstasy</td>
<td>Thinners</td>
<td>GHB</td>
</tr>
<tr>
<td>Hash</td>
<td>Phenmetraline</td>
<td>Freebase</td>
<td>Heroin</td>
<td>LSD (Lisergic acid)</td>
<td>Trichlorethene</td>
<td>Anabolic steroids</td>
</tr>
<tr>
<td>Hash oil</td>
<td>Khat</td>
<td>Coca leaves</td>
<td>Opium</td>
<td>Mescaline</td>
<td>Gasoline/petrol</td>
<td>Laughing gas</td>
</tr>
<tr>
<td></td>
<td>Betel nut</td>
<td></td>
<td></td>
<td>Peyote</td>
<td>Gas</td>
<td>(Halothane)</td>
</tr>
<tr>
<td></td>
<td>Ritaline</td>
<td></td>
<td></td>
<td>PCP, angel dust</td>
<td>Solution</td>
<td>Amyl nitrate</td>
</tr>
<tr>
<td></td>
<td>(Methylphenidate)</td>
<td></td>
<td></td>
<td>(Phencyclidine)</td>
<td>Glue</td>
<td>(Poppers)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Psilocybin</td>
<td></td>
<td>Anticholinergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DMT</td>
<td></td>
<td>compounds</td>
</tr>
</tbody>
</table>

PILLS – MEDICINES

Pills count as drugs when you take

- more of them or take them more often than the doctor has prescribed for you
- pills because you want to have fun, feel good, get "high", or wonder what sort of effect they have on you
- pills that you have received from a relative or a friend
- pills that you have bought on the "black market" or stolen

SLEEPING PILLS/SEDATIVES

<table>
<thead>
<tr>
<th>Alprazolam</th>
<th>Glutethimide</th>
<th>Rohypnol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amobarbital</td>
<td>Halcion</td>
<td>Secobarbital</td>
</tr>
<tr>
<td>Apodorm</td>
<td>Heminevrin</td>
<td>Sobril</td>
</tr>
<tr>
<td>Apozepam</td>
<td>Iktorivil</td>
<td>Sonata</td>
</tr>
<tr>
<td>Aprobarbital</td>
<td>Imovane</td>
<td>Stesolid</td>
</tr>
<tr>
<td>Butabarbital</td>
<td>Mephobarbital</td>
<td>Stilnoct</td>
</tr>
<tr>
<td>Butalbital</td>
<td>Meprobamate</td>
<td>Talbutal</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>Methaqualone</td>
<td>Temesta</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Methohexital</td>
<td>Thiamyl</td>
</tr>
<tr>
<td>Dormicum</td>
<td>Mogadon</td>
<td>Thiopental</td>
</tr>
<tr>
<td>Ethchlorvynol</td>
<td>Nitrazepam</td>
<td>Triazolam</td>
</tr>
<tr>
<td>Fenemal</td>
<td>Oxascand</td>
<td>Xanor</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>Pentobarbital</td>
<td>Zopiklon</td>
</tr>
<tr>
<td>Fluscand</td>
<td>Phenobarbital</td>
<td></td>
</tr>
</tbody>
</table>

PAINKILLERS

<table>
<thead>
<tr>
<th>Actiq</th>
<th>Durogesic</th>
<th>OxyNorm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocciolina-Etyfin</td>
<td>Fentanyl</td>
<td>Panocod</td>
</tr>
<tr>
<td>Citodon</td>
<td>Ketodur</td>
<td>Panocod forte</td>
</tr>
<tr>
<td>Citodon forte</td>
<td>Ketogan</td>
<td>Paraflex comp</td>
</tr>
<tr>
<td>Dexodon</td>
<td>Kodein</td>
<td>Somadril</td>
</tr>
<tr>
<td>Depolan</td>
<td>Maxidon</td>
<td>Spasmofen</td>
</tr>
<tr>
<td>Dexofen</td>
<td>Metadon</td>
<td>Subutex</td>
</tr>
<tr>
<td>Dilaudid</td>
<td>Morfin</td>
<td>Temgesic</td>
</tr>
<tr>
<td>Distalgesic</td>
<td>Nobligan</td>
<td>Tiparol</td>
</tr>
<tr>
<td>Dolcontin</td>
<td>Norflex</td>
<td>Tradolan</td>
</tr>
<tr>
<td>Doleron</td>
<td>Norgesic</td>
<td>Tramadol</td>
</tr>
<tr>
<td>Dolotard</td>
<td>Opidol</td>
<td>Treo comp</td>
</tr>
<tr>
<td>Doloxene</td>
<td>OxyContin</td>
<td></td>
</tr>
</tbody>
</table>

Pills do NOT count as drugs if they have been prescribed by a doctor and you take them in the prescribed dosage.
In the questionnaire that you completed as part of this study, you indicated that you have higher than average levels of stress. Over time, elevated stress levels may negatively impact your daily life. Participation in this study may help you manage your stress levels, however, you may also wish to seek additional counseling or treatment on your own by consulting your family physician or a health care provider of your choice. For your reference, the following is a list of some of the resources in the community that provide mental health counseling and treatment.

<table>
<thead>
<tr>
<th>Outcomes Inc.</th>
<th>Presbyterian Healthcare Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employee Assistance Program</td>
<td>Presbyterian Behavioral Health</td>
</tr>
<tr>
<td>1503 University Blvd. NE</td>
<td>1325 Wyoming Blvd NE</td>
</tr>
<tr>
<td>Albuquerque, NM 87102-1708</td>
<td>Albuquerque, NM 87112-5046</td>
</tr>
<tr>
<td>(505) 243-2551</td>
<td>(505) 291-5300</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>The University of New Mexico School of Medicine</th>
<th>Lovelace Medical Center</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Practice/Psychiatry Center</td>
<td>Lovelace Behavioral Health</td>
</tr>
<tr>
<td>2400 Tucker NE, MSC09 5040</td>
<td>601 Dr. Martin Luther King Jr. Ave. NE</td>
</tr>
<tr>
<td>1 University of New Mexico</td>
<td>Albuquerque, NM 87102</td>
</tr>
<tr>
<td>Albuquerque, NM 87131-0001</td>
<td>(505) 727-8000</td>
</tr>
<tr>
<td>(505) 272-2165</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Susan P. Kaspi, Ph.D.</th>
<th>Christus St. Vincent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior Therapy Associates</td>
<td>Behavioral Health Services</td>
</tr>
<tr>
<td>9426 Indian School Rd NE, Suite 1</td>
<td>2052 Galisteo Street</td>
</tr>
<tr>
<td>(505)345-6100</td>
<td>Santa Fe, NM 87505</td>
</tr>
<tr>
<td>(505)</td>
<td>(505) 913-4350</td>
</tr>
</tbody>
</table>

**Study Contact Information:**
Sara Newman, Study Coordinator
StressStudy@salud.unm.edu
(505) 272-0280

Sang Kim, Researcher
Dept. of Health, Exercise & Sports Sciences
sangkim@unm.edu
(505) 795-4545
Emergency Risk Evaluation Protocol

Should a participant give any indication of being suicidal, homicidal, or psychotic during an interaction, the following steps are to be taken:

Calmly tell the participant to wait in the assessment room. If someone is available to sit with them, this is ideal. Do not tell the participant that you are calling a psychologist to perform a risk evaluation.

Call the study PI Mark Burge, MD at 951-1465.

The person who conducts the risk evaluation should report the details of the event to the PI. The completed note (see attached) should be kept in the study records.

If a participant is determined to be actively suicidal, homicidal, or psychotic, then campus police should be called to escort them to the UNM psychiatric emergency.

Campus Police may be reached at 277-2241 from a cell phone or 911 from any UNM landline.

If the participant is not at acute risk, they are to be given a list of community resources where they can seek mental health counseling.

Actively suicidal, homicidal, or psychotic participants are to be excluded from the study in order to ensure the safety of participants and staff.

Should the participant require an escort to emergency care, the incident will be reported to PI Mark Burge, MD and to the HRRC as an adverse event.
**MSE:**

Appearance: WNL Grooming and hygiene ok  

Behavior: Friendly, cooperative, and engaged  

Speech: WNL, RRR, Clear and coherent  

Mood and Affect: Pt describes mood as ______________ BDI = _____, Affect full and appropriate  

Thought Process: WNL, linear, logical, goal directed,  

Thought Content: WNL, no AH/VH, no delusions or obsessions  

Insight and Judgment: WNL  

Suicide Risk:  

Primary Risk factors: Axis I d/o, SUD, Axis II d/o, Fam hx of suicide, Past hx of suicide attempt, Recent d/c from Ψ hosp, Developmental trauma  

Demographic Risk: white or native American male over 40, divorced, widowed, or separated  

Environmental Risk: Access to gun, firearm; exposure to model for suicide  

Protective Factors: strong personal support system, strong therapeutic support system, strong faith or belief system opposing suicide as an option  

Acute risk factors: Acute stressors/losses (financial, relationship, employment, physical health, pain, etc), affective system factors (rage, fear, anxiety, shame, loneliness, burdensomeness, depression, pessimism, etc.), Impaired problem solving (dichotomous thinking rigidity)  

Suicidality: hopelessness only, passive wish to die only, thought of ending life – with plan, - with intent, - with means, - with rehearsal behavior, - that are persistent, - that are accompanied by command hallucinations  

Suicide Risk: Initial Plan: Discussed with patient and  

Patient education: 1) confidentiality discussed with pt, 2) cognitive/physical/cultural barriers, 3) motivation/ability/readiness to learn, 4) other
Be part of an important research study on the effects of stress in nurses.

- Are you a nurse at UNM?
- Is job-related stress impacting your professional fulfillment or personal well-being?
- Do you want to reduce your stress levels without medication?
- If you answered YES to these questions, you may be eligible to participate in a research study being conducted at UNM.

The purpose of this research study is to investigate the therapeutic effectiveness of low- to moderate-intensity mind-body exercise on stress.

Benefits include participation in a free 8-week mind-body group exercise class (1 hour, twice weekly). Participants will receive two small stipends for successful completion of the study. No medications will be given.

This study is being conducted at UNM Clinical and Translational Science Center in partnership with the UNM Health, Exercise and Sports Sciences Department.

Please call Sara Newman at (505) 272-0280 or email StressStudy@salud.unm.edu for more information.
Your Name:

# Home Exercise Log

<table>
<thead>
<tr>
<th>Date (MM/DD)</th>
<th>Total Minutes (30, 45, 60, 75, etc.)</th>
<th>Type of Exercise (Example: walking, jogging, swimming, weight training, fitness class etc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>
Examples of mind-body stretching and breathing exercises.

Exercises used in the study are a combination of deep breathing and movements from yoga, tai chi, and qigong.

1. Diaphragm toning
2. Finger pressing
3. Rising sun
4. Buddha stretch
5. Head rest
6. Downward dog
7. Cross leg
8. Torso twist
9. Side push
10. One leg balancing